No. 11-1423

In the United States Court of Appeals
For the District of Columbia Circuit

COMMUNITIES FOR A BETTER ENVIRONMENT et. al.,

v.

UNITED STATES ENVIRONMENTAL PROTECTION AGENCY,

Petition for Review of Agency Action

PETITIONERS' AND PETITIONER-INTERVENOR'S CORRECTED OPENING BRIEF

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ORAL ARGUMENT NOT SCHEDULED

UNITED STATES COURT OF APPEALS
FOR THE DISTRICT OF COLUMBIA CICUIT

COMMUNITIES FOR A BETTER ENVIRONMENT and WILDEARTH GUARDIANS, Petitioners, v. UNITED STATES ENVIRONMENTAL PROTECTION AGENCY, Respondent.	Case No. 11-1423

CERTIFICATE AS TO PARTIES, RULINGS, AND RELATED CASES

Pursuant to the Court Order of the United States Court of Appeals for the District of Columbia Circuit issued on November 4, 2011, and D.C. CIR. R. 12(c) and 28(a)(1), Petitioners submit the following certificate as to parties, rulings, and related cases.

(A) **PARTIES AND AMICI**

This is a Petition for direct review by this Court of an administrative rulemaking by the U.S. Environmental Protection Agency taken under 42 U.S.C. §7607(b)(1). Accordingly, there were no parties or *amici* in prior District Court proceedings. The parties to the current proceedings are:

1. Petitioner Communities for a Better Environment

Communities for a Better Environment ("CBE") is a non-profit environmental health and justice advocacy organization with offices in Oakland and Huntington Park, California. CBE's mission is to achieve environmental health and justice by building grassroots power in and with communities of color and working-class communities. In pursuit of its mission, CBE works to secure clean air and reduce pollutant emissions in its members' communities. CBE, along with WildEarth Guardians and others, filed timely formal comments on the EPA's rulemaking at issue in this case.

2. Petitioner WildEarth Guardians

WildEarth Guardians is a non-profit environmental organization dedicated to protecting and restoring the wildlife, wild places, and wild rivers of the American West. WildEarth Guardians has over 8,500 members who reside throughout the United States, mostly in the western U.S. Along with CBE and others, WildEarth Guardians filed timely formal comments in the National ambient Air Quality Standard ("NAAQS") rulemaking for CO at issue in this case. WildEarth Guardians' members are committed to protecting the natural wild aspects of the American West, which are severely affected by climate change. WildEarth Guardians' members who visit the wild places of the west have an interest in protecting such places from global warming.

3. Intervenor Sierra Club

Sierra Club is a nonprofit public-benefit corporation with more than 700,000 members in the United States and with one or more chapters in every state. The Sierra Club's mission is to promote and practice responsible use of the earth's ecosystem and resources; to educate and enlist humans to protect and restore the natural and human environment, and to use all lawful means to achieve these objectives. Sierra Club activities include hiking, canoeing, caving, swimming, fishing, nature study, and advocacy for the improvement and protection of water and air quality across the country. Sierra Club members live, work, recreate, and engage in economic activities in and around areas that are impacted or will be impacted by CO pollution.

4. Respondent Environmental Protection Agency

The Environmental Protection Agency ("EPA") is an agency of the federal government, created with the mission to protect human health and the environment. The current administrator of the EPA is Lisa Jackson. Under the Clean Air Act ("CAA"), EPA is charged with setting NAAQS for air pollutants that "cause or contribute to air pollution which may reasonably be anticipated to endanger public health and welfare." 42 U.S.C. §7408. EPA determined that CO met this standard and completed a court ordered rulemaking on the NAAQS for

CO on August 31, 2011. Review of National Ambient Air Quality Standards for Carbon Monoxide, Final Rule, 75 Fed. Reg. 54294, 54297-98 (Aug. 31, 2011).

(B) **RULINGS UNDER REVIEW**

This case is properly in the United States Court of Appeals for the D.C. Circuit pursuant to 42 U.S.C. §7607(b)(1). It is an appeal of a final rule promulgated pursuant to 42 U.S.C. §7408, published by the EPA, in the Federal Register on August 31, 2011, at 76 Fed. Reg. 54294-01. A copy of EPA's ruling is attached hereto.

(C) **RELATED CASES**

In 2006, EPA was sued by Petitioner Communities for A Better Environment, Rocky Mountain Clean Air Action, Coalition for a Safe Environment, and Physicians for Social Responsibility because it had failed to conduct a five-year review of the CO NAAQS. *Cmtys. for a Better Env't, v. U.S. EPA*, 2008 WL 1994898 (N.D. Cal. 2008). Though not the same case, that case resulted in a Summary Judgment finding in favor of the plaintiffs, and the court ordered rulemaking that is at issue in this case. To the best knowledge of counsel there are no other cases pending before this Court or any other court involving substantially the same issues.

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GLOSSARY

ALA – American Lung Association

APA – Administrative Procedure Act

AQCD – Air Quality Criteria Document

CAA – Clean Air Act

CAD – Coronary Artery Disease

CASAC – Clean Air Scientific Advisory Committee

CH_4 – Methane

CNS – Central Nervous System

CO – Carbon Monoxide

CO_2 – Carbon Dioxide

COHb – Carboxyhemoglobin

CVD – Cardiovascular Disease

HO – Heme Oxygenase

IRP – Integrated Plan for Review (“Plan”)

ISA – Integrated Science Assessment

NAAQS – National Ambient Air Quality Standard

O_3 – Ozone

OH – hydroxide

PA – Policy Assessment

PM – Particulate Matter

PPM – Parts Per Million

REA – Risk Exposure Assessment

STATEMENT OF JURISDICTION

Pursuant to Section 307(b)(1) of the Clean Air Act ("CAA"), 42 U.S.C. § 7607(b)(1), and Rule 15(a) of the Federal Rules of Appellate Procedure, Petitioners and Petitioner-Intervenor seek review of the Environmental Protection Agency's ("EPA") most recent National Ambient Air Quality Standard for Carbon Monoxide ("NAAQS") rulemaking (hereinafter "Final Rule"). Section 307(b) provides that "[a] petition for review of action of [the EPA] in promulgating any national primary or secondary ambient air quality standard . . . may be filed only in the United States Court of Appeals for the District of Columbia." 42 U.S.C. §7607(b)(1). This petition was filed in accordance with Fed. R. App. Proc. 15.

STATEMENT OF ISSUES

I. Whether EPA failed to set a NAAQS that "accurately reflect(s) the latest scientific knowledge useful in indicating the kind and extent of all identifiable effects on public health", when it chose not to consider available information regarding health effects resulting from CO exposure, including, but not limited to: epidemiological studies, sensitive population studies, multi-pollutant studies and co-pollutant studies?

II. Whether EPA violated the CAA requirement to "set forth or summarize and provide a reference to any pertinent findings, recommendations, and comments by the Scientific Review Committee… and, if the proposal differs in any important respect from any of these recommendations, to provide an explanation of the reasons for such differences" when it disregarded, without adequate explanation, the recommendations of the Clean Air Scientific Advisory Committee?

III. Whether EPA met its obligation to protect public health "within an adequate margin of safety" when it concluded the current primary NAAQS for Carbon Monoxide ("CO"), "avoids unacceptable risks"?

IV. Whether EPA violated the CAA when it failed to set a secondary standard for CO, when, as this court has previously recognized, the CAA requires the EPA "act as soon as it has enough information to anticipate effects on public welfare"?

STATEMENT OF FACTS

A. The Clean Air Act's National Ambient Air Quality Standards

Congress enacted the 1970 Clean Air Act ("CAA") Amendments as "a drastic remedy to what was perceived as a serious and otherwise uncheckable problem of air pollution." *Union Elec. Co. v. EPA*, 427 U.S. 246, 257 (1976). At the center of Congress' strategy to address air pollution in the comprehensive program set forth in Title 1, Part A, Sections 106 thru 110 of the CAA, to prevent negative impacts associated with the emissions of common air pollutants into the ambient air. *See* 42 U.S.C. § 7401-7411. Congress based the program on cooperation between the states and the federal government. The federal government, through the EPA, must identify which common air pollutants, referred to as "criteria pollutants," should be regulated to protect public health and the environment. *Id.* at § 7408. Section 108 directs EPA to publish a list of air pollutants that produce emissions that "cause or contribute to air pollution which may reasonably be anticipated to endanger either public health or welfare." *Id*. at § 7408(a)(1). For each criteria pollutant, EPA must prepare an "air quality criteria document ("AQCD")" that collects and presents information "reflect[ing] the latest

scientific knowledge useful in indicating the kind and extent of all identifiable effects on public health or welfare which may be expected from the presence of such a pollutant in the ambient air, in varying quantities." 42 U.S.C. § 7408(a)(2). Relying on the AQCD, EPA then must promulgate primary and secondary NAAQS for the criteria pollutants. 42 U.S.C. § 7409(a).

A primary NAAQS is one "the attainment and maintenance of which in the judgment of the Administrator, based on such criteria and allowing an adequate margin of safety, are requisite to protect the public health." *Id*. at § 7409(b)(1). An adequate margin of safety protects against harms that may not be clearly uncovered, particularly to the most sensitive Americans. *Am. Lung Ass'n v. EPA,* 134 F.3d 388, 389 (D.C. Cir. 1998); *Am. Farm Bureau Fed'n v. EPA*, 559 F.3d 512, 526 (D.C. Cir. 2009); *Lead Indus. Ass'n v. EPA*, 647 F.2d 1130, 1153-54 (D.C. Cir. 1980) (Congress's directive requires EPA to provide protection against harms even where such harm is [not conclusively demonstrated.]).

A secondary NAAQS is one "the attainment and maintenance of which [is] requisite to protect the public welfare from any known or anticipated adverse effects . . . ." 42 U.S.C. § 7409(b)(2). The term "welfare" includes effects on climate. *Id*. at §7602(h).

Once EPA promulgates the NAAQS, states, or Indian tribes where appropriate, are obligated to designate air quality control regions ("AQCR") within

their boarders. *Id*. at §7407. Once established, the state or tribe must determine, cooperatively with EPA, whether each AQCR is in attainment or non-attainment with each NAAQS. *Id*. If an AQCR is in non-attainment, the appropriate state or tribe must prepare a State Implementation Plan for permitting and reducing emissions of criteria pollutants from industrial facilities within the AQCR. *Id*. at § 7410.

EPA must review NAAQS every five years and "make such revisions in such criteria and standards and promulgate such new standards as may be appropriate . . . ." *Id*. at § 7409(d)(1).

B. Carbon Monoxide.

EPA has listed only six criteria pollutants; one of which is Carbon Monoxide ("CO"). CO is a colorless, odorless gas produced primarily through incomplete combustion of fossil fuels. (Joint Appendix ("JA") __) EPA-HQ-OAR-2008-0015-0187(54279).[1] CO is also produced within human bodies through the routine breakdown of heme proteins. CO is deadly to humans at high levels, and causes serious adverse health effects at lower levels. *Id.*(54299).

CO interacts with the human body through "several pathways." *Id.* One pathway is through the cardiovascular system. *Id.*(54298). CO interacts with

[1] Petitioners contacted opposing counsel offering to use one set of bates numbers for record citations. Opposing counsel declined. Petitioners are citing to EPA's docket (with pin cite in parentheses) until the deferred joint appendix is compiled, pursuant to this Court's Order. Communities for a Better Environment v. EPA, No. 11-1423 (Dec. 9, 2011).

hemoglobin in the blood and forms carboxyhemoglobin ("COHb"), which even at very low levels reduces oxygen consumption in tissues. *Id.*(54298). Inhaled CO is quickly absorbed into arterial blood (blood transported through arteries). *Id.* While in arteries, CO combines with hemoglobin to form arterial carboxyhemoglobin, ("(a)COHb"). Decl. of Albert Donnay, Addendum B (hereinafter "Donnay") at ¶32-38. Along with arterial blood, via (a)COHb, CO is transported to body tissue. *Id*. There, it mixes with endogeneous CO, already present in the body. This CO mixture removed slowly from tissues through venous blood (blood transported through veins), becoming (v)COHb, and is then exhaled through the lungs. *Id.*

(a)COHb and (v)COHb are two different biomarkers of CO exposure. *Id*. at ¶36-37. Neither (a)COHb or (v)COHb alone indicate dose[2] to tissues. *Id.* Many authors of clinical studies, as well as EPA in the Final Rule, conflate and confuse the terms. *See, e.g.*, (JA__) EPA-HQ-OAR-2008-0015-0187 (referring only to the singular term COHb and never mentioning this significant distinction). Using the two interchangeably can lead to misleading results that are difficult, if not impossible, to replicate and should not be relied on. *See generally*, (JA__) EPA-HQ-OAR-2008-0015-0179. If COHb is used to measure exposure, in other words the amount of CO which diffuses into tissues, it "can… only [be measured] by

[2] Dose is a measure of the amount of COHb transported to and from tissues.

repeated measures of both arterial and venous COHb, from which the critically important diffusion gap between them can be estimated." *Id.* This is an ineffective way to measure CO exposure because (v)COHB levels in particular rise very slowly, taking at least 24 hours to reach equilibrium. Donnay at ¶38-41.

CO also acts through other pathways in the body, "which involve a wide range of molecular targets and internal CO concentrations," some of which are still not fully understood. *Id.* One such pathway is the various interactions of endogenous CO, and its primary source heme oxygenase ("HO"), through human biological systems. (JA __) EPA-HQ-OAR-0015-179(27). "Once CO is inhaled from any exogenous source . . . it mixes with endogenous CO (CO created in the body) and becomes indistinguishable from CO created in the body." *Id.* This, and other pathways, affects the cardiovascular, respiratory, and central nervous systems, as well as human development. *Id.* As discussed below, these effects are not well documented in the clinical CO studies relied upon by EPA, but have been documented through epidemiological evidence. Donnay at ¶49-51.

CO also has direct and indirect impacts on Earth's atmosphere that cause an increased greenhouse effect, and consequently, contributes to global climate change. Scientific reports relied upon by EPA concluded that, "a causal relationship exists between current atmospheric concentrations of CO and effects on climate." (JA __) EPA-HQ-OAR-2008-0015-0187(16). CO "absorbs outgoing

thermal infrared radiation." (JA __) EPA-HQ-OAR-2008-0015-0174(8). The heat retained by the CO remains in the atmosphere until the CO dissipates, which has a direct impact on climate change. *Id*. More significantly, CO has two major indirect effects on climate. *Id.* First, CO reacts with hydroxide ("OH") – a compound that removes greenhouse gases ("GHGs") from the atmosphere. (JA __) EPA-HQ-ORD-2007-0925-0017(3-11). Therefore, when CO removes OH from the atmosphere there is less OH available to remove other GHGs from the atmosphere. *Id.* Second, the interaction between CO and OH forms three important GHGs: carbon dioxide ("CO_2"), methane ("CH_4"), and ozone ("O_3"), which absorb infrared radiation from Earth's surface and contribute to the greenhouse effect directly. *Id.* Globally, the indirect "effect of CO is about 25 percent of the 20-year influence of CO_2." (JA __) EPA-HQ-OAR-2008-0015-0174(9).

C. The National Ambient Air Quality Standard for Carbon Monoxide.

EPA set the primary CO NAAQS in 1971 at 9 parts per million (ppm) average over an 8-hour period, and 35 ppm average over a 1-hour period. (JA ___) EPA-HQ-OAR-2008-0015-0187(54295). EPA reviewed this standard in 1980, 1985, and 1994. In 1980, EPA proposed to lower the 8-hour standard from 35 to 25, but no final rule was published. *Id*. Instead, in 1985 and 1994, EPA retained

the 1971 standard. In the last 40 years the standard has not been revised, despite advances in science showing harmful effects of CO exposure. Donnay at ¶14.

1. <u>Types of CO studies</u>

There are three types of scientific studies relevant to EPA's consideration of the CO NAAQS: clinical, toxicological, and epidemiological. (JA __) EPA-HQ-ORD-2007-0925-0017(45). There are subsets of each of these broader categories. For instance, review studies which analyze multiple studies on similar issues and summarize the results, and CO poisoning studies that analyze the effects of high levels of CO exposure. (JA ___) EPA-HQ-OAR-2008-0015-0179(16, 28-31).

EPA principally relied on six clinical studies on cardiac effects, and characterized other evidence on the health effects as "limited." (JA __) EPA-HQ-OAR-2008-0015-0187(54299). Clinical studies rely on COHb—particularly, (v)COHb—as the biomarker for CO exposure, which EPA calls "the best characterized mechanism of action of CO." *Id.*(54298). All six clinical studies reviewed by EPA measure COHb levels after 1-4 hours of exposure to CO concentrations of 50 to over 200 ppm. EPA-HQ-OAR-2008-0015-0179(3); *see also* Donnay at ¶71, Table 1. Each clinical study uses the same measurement (co-oximetry), to measure COHB levels. Donnay at ¶94. EPA claims, "as a group, these studies demonstrate . . . the susceptibility of people with CAD to incidents of exercise-associated myocardial ischemia." (JA __) EPA-HQ-OAR-2008-0015-

0187(54300). It is worth noting, however, all six studies presented inconsistent results with regard to COHb levels and the amount of time until cardiac effects presented.[3] Donnay at ¶94; Donnay at ¶71, Table 1.

EPA placed "principal emphasis" on a 1989 clinical study, commonly referred to as the Allred study. (JA __) EPA-HQ-OAR-2008-0015-0187(54300). EPA cites this study over 30 times in the Final Rule. The Allred study "evaluated changes in time to exercise-induced onset of markers of myocardial ischemia resulting from two short (approximately 1-hour) CO exposures targeted to result in mean study subject COHb levels of 2% and 4%, respectively." *Id.*

Several concerns have been raised with the Allred study. For example, the study "included only 63 non-smoking men as subjects." Donnay at ¶53; *see also* (JA __) EPA-HQ-OAR-2008-0015-0177(5). Moreover, all of the exposure levels and most of the total doses used in the Allred study upon which EPA primarily relies were greater than the current average 1-hour limit of 35ppm. (JA __) EPA-HQ-OAR-2008-0015-0179(3). The average exposure ranged from 42ppm to 357ppm. *Id.* The high-end of this range is over 10 times the exposure allowed by EPA's 1-hour CO NAAQS, providing little basis for understanding public health impacts at lower doses. *Id.* The study exposed subjects to these various levels for only 50-70 minutes. *Id.* It appears, the goal of the study was for each subject to

[3] The studies specifically measured the decrease in time to angina. Donnay at ¶70, Figure 4.

reach the same target levels of (v)COHb, essentially either 2% or 4%. Donnay at ¶24,31.

By tying results to COHb levels after short-term exposure, the study does not reflect health effects of CO exposure at the current standard and lower. Donnay at ¶43-47. The study reports a wide range of individual results, both positive and negative. (JA __) EPA-HQ-OAR-2008-0015-0177(6). Despite these limitations, EPA uses Allred to justify maintaining the current standard. *See generally*, (JA __) EPA-HQ-OAR-2008-0015-0179.

Not only is the Allred study flawed in a variety of ways, but it is also outdated. Donnay at ¶24-31, 55-70. In the last two decades thousands of new studies demonstrate health effects of CO at low levels. Donnay at ¶14. Many of these are epidemiological studies. EPA acknowledges the epidemiological evidence has "expanded considerably" in recent decades. (JA __) EPA-HQ-OAR-2008-0015-0187(54300). In the 18 years since the last review, there have been "many statistically significant epidemiological findings of increased morbidity and mortality risks from small increases in outdoor CO exposure at levels below the current NAAQS." (JA __) EPA-HQ-OAR-2008-0015-0177(10). The American Lung Association ("ALA") agreed stating, that "evidence for harm to lung health has grown since the 1994 and 2000 reviews . . . ." (JA __) EPA-HQ-OAR-2008-0015-0181(7).

The ALA highlighted ten epidemiological studies published in the last ten years that showed increased hospital and emergency room admissions for children and the elderly with respiratory problems, particularly asthma and adults with respiratory issues. *Id.*(8). ALA further cites epidemiological studies published in 2006 and 2007 that found that "CO was significantly associated with asthma hospital admissions," and "emergency department visits for children 16 and under," respectively. *Id.*(9). These studies led ALA to conclude that "multiple large epidemiological studies have found strong associations with exposure to CO and serious documented respiratory health endpoints . . .." *Id.*

Epidemiological evidence published since 2000 demonstrates the relationship between CO and a wide range of health effects. These studies, which were cited in comments, demonstrated over 70 health effects. (JA __) EPA-HQ-OAR-2008-0015-0179(10). Numerous studies cited in comments, show effects on the development and respiratory health of children as well as various types of hospital visits and mortality and morbidity in adults. *Id.* Further, 22 epidemiological studies that all showed a significant increased risk of developing serious medical conditions associated with small increases in CO exposure. Donnay at ¶111, Table 3. Most significant is the increased risk of 195% for cardiac birth defects in fetuses. Donnay at ¶111.

Because epidemiological studies do not rely on COHb measurements, other CVD effects, as well as other effects not measured by clinical studies, can be shown at much lower levels. *Id. See also* Donnay at ¶125-125. The current state of CO research is analogous to research on lead exposure a few years ago, when lower overall ambient lead levels allowed researchers to discover, through epidemiological research, that very low levels of chronic exposure are more dangerous than higher levels. *Id.*

Similarly, scientific knowledge about CO effects has expanded since 2000, particularly in areas such as CO poisoning and review studies. CO poisoning studies analyze "adverse outcomes seen after acute CO poisoning at levels much higher than the CO NAAQS." *Id.* CO poisoning studies are useful in understanding how inhaled CO might be a better clinical indicator of exposure than COHb. *Id.* These studies "demonstrate effects on organs and bodily functions of children and adults at levels **above** current ambient exposure levels." *Id.* (emphasis added). However, the data is also supportive of similar observed effects at lower levels of exposure. Donnay at ¶131. These studies demonstrate effects on the cardiovascular, respiratory, and central nervous systems of children, lending credibility to epidemiological studies of these same effects. (JA__) EPA-HQ-OAR-2008-0015-0179(15); Donnay at ¶111, Table 3. Similarly, recent CO poisoning research on adults support the findings of epidemiological studies and

"should lead EPA to broaden the range of CO effects [of concern] at levels below the current NAAQS." *Id*.

The number of review studies published in the last 10 years has also expanded. Donnay at ¶138. Many review studies investigate the ways in which endogenous HO and CO are active in the body. *Id.* These studies have led medical researchers to recognize that "endogenous CO is bioactive at very low concentrations." *Id.* Interestingly, one review reports effects of endogenous CO on vascular tone, atherosclerosis, pregnancy, reproductive hormones, male reproductive function, liver function, stress response, nerve transmission and immune response. Donnay at ¶136. Over 100 other review studies found correlations to effects on "critically important neurological, immunological, muscular, digestive, reproductive, sensory, and metabolic pathways." *Id.* Further, researchers now recognize that "[e]very passing week brings new knowledge about the systems in which CO acts." Donnay at ¶136 (citing Morse D, Sethi J, *Carbon Monoxide and human disease*, 2 Antioxid Redox Signal 331-8 (2002)).

D. EPA's 2011 Rulemaking and the Current Petition for Review.

After its 1994 review, EPA began the NAAQS review process and created an AQCD in 2000. (JA__) EPA-HQ-OAR-2008-0015-0187(54296). However, EPA never issued the proposed rule based on that AQCD. In 2006, Petitioner Communities for A Better Environment ("CBE") and other groups sued EPA

because it failed to conduct a five-year review of the CO NAAQS. *Cmtys. for a Better Env't v. U.S. EPA*, 2008 WL 1994898 (N.D. Cal. 2008). The court granted Petitioners' motion for summary judgment and ordered EPA to complete the CO NAAQS review. *Id.* at *6. During this litigation, in September 2007, EPA began its review process. EPA eventually completed the rulemaking on August 31, 2011, published in 76 Fed. Reg. 54294. (JA__) EPA-HQ-OAR-2008-0015-0187(54294).

1. The Review Process

a. Integrated Plan for Review ("Plan")

EPA's Plan for the 2011 CO NAAQS review laid out a new process and relies on five essential documents at corresponding stages: the Integrated Plan for Review ("IRP"), the Integrated Science Assessment ("ISA"); the Policy Assessment ("PA"); the Risk Exposure Assessment ("REA"); and the proposed and final rule. (JA __) EPA-HQ-OAR-2008-0015-0028(1-1). For each document, EPA issued one draft for review and comment by the public and CASAC before EPA published the final document. *Id.*(1-2). The Plan also sets out the EPA's method of collecting and maintaining a database for studies published after 2000 to serve as a reference for the ISA. *Id.*

b. The ISA

The ISA is a new name for the CAA's AQCD. 42 U.S.C. §7408. The ISA is intended as a comprehensive assessment of the "latest scientific knowledge"

relevant to public health and environmental effects of CO exposure. *See* 42 U.S.C. § 7408. The CO ISA contains 817 total references, 660 of which were published since 2000. EPA-HQ-ORD-2007-0925-0017(585-593). This is a small fraction of potentially relevant CO studies, particularly since 2000. A general search of CO on PUBMED.com returns "7,849 peer-reviewed studies on CO published in English from 2000 through 2009." Donnay at ¶152.

During review of the proposed final rule, commenters drew attention to 393 studies not covered in the document, including epidemiological, poisoning and review studies, as well as new clinical studies on inhaled CO.

c. The Clean Air Scientific Review Committee

As required by Section 109 of the CAA, EPA appointed CASAC to review the ISA and NAAQS. 42 U.S.C. § 7409(d)(2). CASAC holds a public conference to review each draft of the EPA documents, then offers its own set of findings and recommendations in a series of comment letters to the Administrator. *See e.g.*, (JA__) EPA-HQ-OAR-2008-0015-0029(1). These letters present CASAC's overall comments regarding the drafts and consensus responses to EPA's charge questions. *Id.*

In a June 2010 comment letter regarding the PA, CASAC repeatedly expressed the importance of epidemiologic studies. *See, e.g., id*.(2). In response to a number of charge questions concerning whether proper consideration of

epidemiological studies would change the NAAQS level requisite to protect against adverse health effects, CASAC stated that: "[t]he document does not appear to give epidemiologic studies sufficient standing relative to the controlled human exposure data, even though they may be more realistic" (*id*.(7)); "the presentation [regarding the quantitative analysis of exposure and dose] unnecessarily diminished the value of the epidemiological studies" (*id*.(9)); and "[a]lthough it may be a challenging task, it is important to integrate the evidence from the epidemiological studies with the clinical studies" (*id*.10)). CASAC further noted EPA's integration of evidence from the ISA and draft REA, to conclude that the current standard was adequate were not well supported. *Id.*(10).

Finally, CASAC addressed the adequacy of the current and potential alternative standards, and offered direct recommendations regarding consideration of epidemiological studies and how they directly impact the standard. *Id.* CASAC's panelists agreed that in light of epidemiologic studies presented in the PA, "the current standards may not protect public health with an adequate margin of safety, and therefore revisions that result in a lowering the standards should be considered." *Id.*(11). CASAC noted because further clinical studies of some sensitive groups would be impossible to justify ethically, "more reliance needs to be placed on the epidemiologic studies and assessing whether there are causal relationships," to health effects on sensitive groups. *Id.*(12). CASAC concluded

that "[i]f the epidemiological evidence is given additional weight, the conclusion could be drawn that health effects are occurring at levels below the current standard, which would support the tightening of the current standard." *Id.*(12).

CASAC's overall impressions of the PA reflect its desire that EPA give greater weight to the epidemiologic studies. CASAC stated:

> [T]here was too much dependence on the now classic clinical study conducted by Allred et al. (1989) . . . . While agreeing that this seminal study provided important evidence, its findings should not be so emphasized as to ignore more contemporary epidemiologic studies, especially those directed at coronary artery disease (CAD) and cardiovascular disease (CVD) more generally. The epidemiologic studies are important because other cardiovascular conditions affect a large number of people who are at risk form CO exposure. We support the high level of attention to populations at risk, but continue to be concerned that the Agency is underestimating CO exposure among some vulnerable groups, especially persons with low income status. This is one rationale for placing greater emphasis on the findings of the epidemiologic studies versus the controlled clinical studies . . . . **<u>We recommend this greater emphasis of the epidemiologic data across all of the CO documents.</u>**

Id.(1-2) (emphasis added).

In a May 2010 letter regarding comments to the draft REA, CASAC again expressed concern over the lack weight given to epidemiologic studies, and noted that broader consideration of health outcomes is needed. (JA __) EPA-HQ-OAR-2008 -0015-0034(1-2). In its overall comments, CASAC stated it felt strongly that "the focus of the REA, and the associated [PA] document, should be broader than cardiac ischemia (coronary artery disease or CAD)." *Id.*(1). CASAC

acknowledged that the clinical studies are primarily based on COHb pathways, but also notes that "there is increasing evidence that CO increases the frequency and severity of congestive heart failure and enhances susceptibility to arrhythmias." *Id.*(2). Therefore, CASAC recommended, "that a broad set of health outcomes be considered, beyond cardiac ischemia," such as susceptible populations including "those with pulmonary disease and the fetus." *Id.*

Within the same letter, CASAC maintained that although some members supported a cautious approach to using epidemiological data, there were overall concerns that the epidemiologic findings were underemphasized. *Id.*(8). CASAC stated "[e]ven if the epidemiological data are not used in the [REA], it is important to incorporate them into the discussion of risk" because the epidemiological evidence "provides information on non-hypoxia relevant mechanisms and chronic outcomes that cannot be addressed by relying on COHb levels alone." *Id.* Expanding on its concern with EPA's narrow designation of at-risk populations, CASAC recommended that in light of the epidemiological studies, risk modeling should be expanded to include other susceptible populations. *Id.*

2. <u>The Final Rule</u>

On August 31, 2011, EPA issued a final rule entitled "Review of National Ambient Air Quality Standards for Carbon Monoxide." (JA__) EPA-HQ-OAR-2008-0015-0187(54294). EPA determined that the 1971 primary CO NAAQS

remains protective of public health, and elected not to establish a secondary standard for CO. *Id.*

EPA based the NAAQS on six clinical studies—particularly, the Allred study—to conclude that "[i]n this review, the clearest evidence for ambient CO-related effects is available for cardiovascular effects." *Id.*(54928). EPA identifies people with Coronary Artery Disease ("CAD") as a susceptible population. *Id.* CAD is a subset of the broader category of people with CVD. *Id.* CAD includes those with "angina pectoris (cardiac chest pain), those who have experienced a heart attack, and those with silent ischemia or undiagnosed ischemic heart disease." *Id.*(54299).

EPA noted people with other cardiovascular diseases "are also at risk of CO-induced health effects." *Id.* EPA also agreed that the ISA presents evidence "suggestive of causal relationships between relevant ambient CO exposure and several other health effects: Relevant short and long-term CO exposures and central nervous system ("CNS") effects, birth outcomes and developmental effects following long-term exposure, respiratory morbidity following short-term exposure, and mortality following short-term exposure." *Id.* EPA also lists a number of other populations that are potentially at risk of CO-induced effects, including:

> Those with other pre-existing diseases that may already have limited oxygen availability, increased COHb levels or increased

> endogenous CO production, such as people with obstructive lung diseases, diabetes and anemia; older adults; fetuses during critical phases of development and young infants or newborns; those who spend a substantial time on or near heavily traveled roadways; visitors to high-altitude locations; and people ingesting medications and other substances that enhance endogenous or metabolic CO formation.

Id. EPA then dismissed evidence supporting the susceptibility of these groups as "limited" because the majority comes from epidemiological studies. *Id.*

SUMMARY OF THE ARGUMENT

The current CO NAAQS does not protect public health and welfare. In deciding to maintain the 1971 CO NAAQS, EPA failed to meet its statutory obligations in several ways. First, EPA does not base the primary CO NAAQS on the latest scientific knowledge available. The record before the Court reveals that EPA excluded numerous relevant recent studies on CO health effects that were submitted by outside commenters with expertise in public health. Further, EPA unexplainably relied upon a limited set of clinical studies, while providing no credible explanation why it did not give weight to more recent CO science, including epidemiological studies.

Second, EPA violated the CAA by failing to adopt a primary CO NAAQS that protects public health with an adequate margin of safety. The current standard does not adequately protect those with CAD, does not protect **all** susceptible populations, and does not protect against all ambient CO health effects. The record

is rife with evidence demonstrating that a lower standard is necessary to protect public health, including susceptible populations, with an adequate margin of safety. Clinical and epidemiological studies, CASAC commentary, public comments, and EPA staff commentary all point to the need for a lower CO standard. Because EPA's CO NAAQS is contrary to evidence in the record, its CO standard is arbitrary and capricious.

Third, EPA failed to meet its statutory obligation to summarize CASAC's findings and explain any decision to depart from CASAC's recommendations. EPA dismissed CASAC's preference for a lower standard, and then, mischaracterized CASAC's recommendation by stating a lower standard would be appropriate only if more weight was given to epidemiological studies. In doing so, EPA ignored CASAC's repeated recommendation that the data be given more weight, despite any issues with those studies. In addition, EPA overstates CASAC's agreement with the EPA's conclusion that evidence provides support for retaining the current standard.

Finally, EPA failed to meet its obligation to set a secondary standard for CO as soon as adverse effects on public welfare are known or anticipated. Congress has repeatedly expressed concerns over climate change, which is included in public welfare. Despite evidence in the record that EPA was aware of CO's impacts on

climate, CASAC commentary on the effects of CO on climate change, and commenters concerns, EPA did not set a secondary standard for CO.

EPA's decision to keep the current primary standard and its decision not to set a secondary standard is arbitrary and capricious. Evidence in the record mandates a lower primary standard and the setting of a secondary standard.

STANDING

An organization has standing where:

> at least one of its members would have standing to sue in his own right, (2) the interests the association seeks to protect are germane to its purpose, and (3) neither the claim asserted nor the relief requested requires that an individual member of the association participate in the lawsuit.

Sierra Club v. Envtl. Prot. Agency, 292 F.3d 895, 898 (D.C. Cir. 2002) (citing *Hunt v. Washington State Apple Advertising Comm'n*, 432 U.S. 333, 342-43 (1977)). To satisfy the first requirement, the organization must establish Article III standing for at least one member. *See id*. at 898, 902. Article III standing requires a showing of (1) injury-in-fact; (2) causation; and (3) redressibility. *Lujan v. Defenders of Wildlife*, 504 U.S. 555, 560 (1992).

The challenged rule sets a primary NAAQS that allows the continued exposure of CBE's and WildEarth Guardians ("Guardians") members to levels of CO pollution associated with a variety of adverse health and welfare effects and deprives Petitioners' members the level of health and welfare protection mandated

by the CAA. Decl. of Shana Lazerow in support of CBE's Claim of Standing at ¶7 (attached hereto as Addendum C) (hereinafter "Lazerow"); Decl. of Jeremy Nichols in support of WildEarth Guardians' Claim of Standing at ¶12 (attached hereto as Addendum D) (hereinafter "Nichols"); Decl. of Maxine Oliver-Benson in support of CBE's Claim of Standing at ¶¶6-8 (attached hereto as Addendum E) (hereinafter "Oliver-Benson"). The challenged rule also fails to set a secondary standard that provides protection from adverse effects to the global climate that has a direct effect on the wildlife, fish, and plants that Guardians' Climate and Energy Program works to safeguard. Nichols at ¶5.

CO pollution has a disproportionately high impact on working class communities and communities of color living near heavily trafficked freeways, which is directly related to how air pollution is regulated. Lazerow at ¶7. NAAQS are therefore germane to CBE's mission to achieve environmental justice by building grassroots power in and with communities of color and working class communities. Lazerow at ¶4. Because the welfare-based values that secondary NAAQS are designed to protect include climate change, the NAAQS are germane to Guardians' mission to protect and restore wildlife, wild rivers, wild places in the American West. Nichols at ¶¶ 5, 16.

A favorable ruling, requiring EPA to reconsider the primary CO NAAQS would redress the harms Petitioners' are experiencing by providing a new

regulatory path to lower CO exposure. Oliver-Benson at ¶13. Cleaner air near roadways and lower emissions will allow the Petitioners' members to live longer, healthier lives. Lazerow at ¶12; *see also* Nichols at ¶17. Petitioners' members intend to continue to live, work, and recreate in the areas where they currently do. Without a favorable ruling requiring EPA to reconsider setting a secondary standard, the harms Petitioners' are experiencing will be ongoing. Nichols at ¶17; Lazerow at ¶12; Oliver-Benson at ¶2.

For the foregoing reasons, Petitioners' have standing to bring this action. *See e.g., Natural Res. Def. Council v. EPA,* 464 F.3d 1, 5-7 (D.C. Cir. 2006) (finding an organization had standing on behalf of members to challenge EPA's failure to adopt emission standards required under the CAA).

STANDARD OF REVIEW

Section 706 of the APA provides the standard of review petition for review of an agency action: "to the extent necessary . . . the reviewing court shall decide all relevant questions of law, interpret constitutional and statutory provisions, and determine the meaning or applicability of the terms of an agency action. The reviewing court shall . . . (2) hold unlawful and set aside agency action, findings, and conclusions found to be (A) arbitrary, capricious, an abuse of discretion, or otherwise not in accordance with law." "[t]he agency must examine the relevant data and articulate a satisfactory explanation for its action including a 'rational

connection between the facts found and the choice made.'" *Motor Vehicle Mfrs. of U.S., Inc. v. State Farm Mut. Auto. Ins. Co.*, 463 U.S. 29, 43 (1983). The United States Supreme Court has stated that an agency action fails to meet this standard when it: 1) relies on factors not contemplated by Congress; 2) entirely fails to consider an important aspect of the problem; 3) offers an explanation for its decision that runs counter to the evidence considered; and/or 4) offers an explanation that is so implausible that it could not be ascribed to agency expertise. *Id.* In reviewing NAAQS, this Court has held EPA's failure to explain how public health and welfare are protected to be arbitrary and capricious. *Am. Farm*, 559 F.3d at 520.

ARGUMENT

I. EPA failed to set a CO NAAQS that "accurately reflect(s) the latest scientific knowledge useful in indicating the kind and extent of all identifiable effects on public health.

A. EPA failed to explain why it ignored relevant recent studies.

EPA failed to include hundreds of recent studies on the harmful effects of CO in the ISA for the challenged rulemaking. By excluding relevant studies from the ISA, EPA not only shirked its statutory obligation, but kept relevant information out of the hands of CASAC and the public. That information could have contributed to a dialogue about the proper NAAQS standard to protect public health.

This Court has acknowledged a degree of deference to EPA's scientific judgment. *See Am. Farm Bureau Fed'n v. E.P.A.*, 559 F.3d 512, 520 (D.C. Cir. 2009). The Court has not, however, addressed whether EPA should be given deference in choosing which scientific studies to include in its review of a NAAQS. Certainly, deference should be accorded to EPA when the agency has reviewed **all** relevant studies and made a reasoned and explained scientific judgment about those studies in setting a NAAQS. But where, as here, EPA not only failed to consider relevant studies in reviewing a NAAQS, but provided no reasoned explanation why, deference to the agency's ultimate decision is not warranted. To give deference in this latter circumstance would ignore Congress' express desire that EPA must make its decision based on "the latest scientific knowledge," 42 U.S.C. § 7408; *see Chevron, U.S.A., Inc. v. Natural Res. Def. Council, Inc.*, 467 U.S. 837, 844 (1984).

In this regard, Congress makes clear in the House Report accompanying the CAA amendments that the purpose of the act is "to assure regulatory action can effectively prevent harm before it occurs." *Lead Industries Association v. EPA*, 647 F.2d 1130, 1152 (D.C.Cir.1980) (citing H.R. Rep. No. 95-294 (1977) (Conf. Rep.)). When considered in this context, one could infer Congress intended latest scientific knowledge to include the **most recent** studies related to each NAAQS. Further, when construed in the context of EPA's obligation to conduct five-year

reviews, the word "latest" can only be read to include those studies since the last statutory review. *See* 42 U.S.C. § 7409. EPA seems to have agreed, at least in formulating its Plan for the most recent CO NAAQS review, in stating that the focus of the ISA would be on studies published since the last review and the 2000 AQCD. (JA __) EPA-HQ-ORD-2007-0925-0017(8). However, when it came to the actual rulemaking, EPA inexplicably, and clearly contrary to the most recent scientific thinking,[4] chose to exclude from the ISA numerous studies suggesting that the current CO standard might not be sufficient to prevent negative health effects of CO. Donnay at ¶14, 106-145.

Among the studies ignored by EPA were epidemiological studies, CO poisoning studies, review studies, and new clinical studies. Comments to the draft NAAQS highlighted at least 46 epidemiological studies not cited in the ISA, and for which there seems to be little or no evaluation by EPA in the record. Donnay¶114.[5] These studies, **<u>all</u>** published after 2000, cover a wide range of

[4] The ISA contains 817 citing references, over 150 of which were published before 2000, and some date back to the 1960s. *See* (JA__) EPA-HQ-ORD-2007-0925-0017. According to testimony presented to EPA, Cynthia George, PhD, found "the ISA considered only 9% of over 8,000 peer reviewed articles published since 2000." (JA __) EPA-HQ-OAR-2008-0015-0164(3). Even this testimony may be generous. There are 660 studies published since 2000 cited in the ISA. *See* (JA __) EPA-HQ-ORD-2007-00925-0017. This puts the percentage of available recent studies cited by EPA in the ISA at just under 8%.

[5] As discussed in Parts I.B and I.C, *infra*, the administrative record in this case, and in particular the comment letters from experts in the field of public health (the American Lung and Heart Associations; Physicians for Social Responsibility, etc.) amply document the availability of epidemiological studies, CO poisoning studies, scholarly review studies, and other more recent clinical studies that address the adequacy of the current CO NAAQS to protect public health.

health effects. (JA__) EPA-HQ-OAR-2008-0015-0179(9-15); EPA-HQ-2008-0015-0181(9). They discuss dozens of CO-related symptoms and syndromes including cardiovascular and respiratory diseases, schizophrenia, and mortality. (JA__) EPA-HQ-OAR-2008-0015-0179(9-15); EPA-HQ-2008-0015-0181(9). Further, the studies show effects on every age group from infants to the elderly. Donnay at ¶111, Table 3.

Epidemiological studies are important to EPA's review for two reasons. First, they shed light of the deficiencies of the clinical studies EPA relies on. Donnay at ¶91-111. (JA __) EPA-HQ-OAR-2008-0015-0179(9). Because epidemiological studies use a different exposure/dose metric than COHb, they are

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The record before the Court lacks, however, any reasoned explanation for EPA's decision to essentially give no weight to these studies and instead rely on increasingly outdated (and discredited) clinical studies. EPA instead made only a cursory assertion that it considered the more recent scientific information to be "limited." (JA__) EPA-HQ-OAR-2008-0015-0187. Give the lack of explanation by EPA, Petitioners are submitting in support of their Petition for Review the Declaration of Mr. Albert Donnay, who has more than 14 years of experience researching, writing and speaking about CO-related issues, and is currently a doctrinal student at the University of Maryland. Petitioners are not submitting Mr. Donnay's declaration as substantive evidence to refute EPA's decision to maintain the current CO NAAQS. Instead, Mr. Donnay's testimony seeks to explain the importance of the excluded studies, and why procedurally EPA's decision to exclude them violates the agency's statutory obligation under 42 U.S.C. §7408. In short, paragraphs 71-145 of Mr. Donnay's declaration shed light on EPA's inadequate explanation of its decision in record before the Court and how the agency failed to consider factors relevant to its decision under the CAA, both of which are permissible uses of non-record evidence in an APA case. *Esch v. Yeutter*. 876 F.2d 976, 991-92 (D.C. Cir. 1989); *IMS, P.C. Alverez*, 129 F.3d. 618, 624 (D.C. Cir. 1997). Other portions of Mr. Donnay's declaration, for example paragraphs 19-70 and 146-199, are proffered for the limited purpose of shedding light on some of the more complex technical issues before the Court and are not intended as substantive evidence. *Esch*, 876 F.2d at 991-92.

of greater significance than those of controlled studies such as Allred. Donnay at ¶20-21; 112. Epidemiological studies are focused—by design—on evaluating the effects of toxic exposures at current ambient levels, not concentrations established in a clinical setting designed to elicit a response in the subject. *Id.* at ¶124-125.

CO poisoning studies are particularly important and relevant to the CO NAAQS review. They support the epidemiological evidence of effects at ambient levels. (JA __) EPA-HQ-OAR-2008-0015-0179(16); Donnay at ¶127-132. In fact, one commenter presented EPA with 25 CO poisoning studies demonstrating effects on infants, neonates, and children. *Id*.(17-27). These studies not only showed cardiovascular effects on children, but also reported "neurocognitive and neuropsychological effects, sensory effects, altered cerebrovascular circulation, and even cerebral palsy from poisoning in utero." *Id*.(16). In addition, "[i]mpaired fetal growth is associated with very low levels of maternal exposure." *Id.*

CO poisoning studies that report on multiple individuals also highlight differences in the effects of CO on different populations, such as differences between children and the elderly, or men and women. Donnay at ¶132. Over 100 of the CO poisoning studies ignored by EPA demonstrate at least 15 different negative effects in adults beyond cardiovascular effects. (JA __) EPA-HQ-OAR2008-0015-0179(16-27); Donnay at ¶127-132. Further, these studies "may

also identify various risk and protective factors of relevance to ambient exposures." Donnay at ¶132.

Finally, EPA excluded 143 scientific review studies. Donnay at ¶133. Scientific review studies are relevant because they can gather and analyze the results of multiple similar studies and summarize the results. (JA __) EPA-HQ-OAR2008-0015-0179(28-40); *see also* Donnay at ¶133-41. Particularly in rapidly growing areas of science like endogenous CO, review studies can highlight similarities in how CO acts in different areas and pathways in the human body. Donnay at ¶135.

Many review studies dismissed by EPA, "discuss studies that have investigated the many ways in which endogenous HO and CO are bioactive . . . in many critically important neurological, immunological, muscular, digestive, reproductive, sensory, and metabolic pathways." EPA-HQ-OAR-2008-0015-0179(28). These studies could help EPA understand the other pathways through which CO works in the body, as EPA currently believes there is not enough evidence regarding these pathways. *See* EPA-HQ-OAR-2008-0015-0187(54298); Donnay at ¶¶135-39. Evidence of these new pathways also refutes EPA's contention that COHb is the only understood pathway in which CO acts in the body. *Id*. Some of the review studies analyze delayed effects of CO exposure, which should also be of concern to EPA. (JA __) EPA-HQ-OAR02008-0015-

0179(28). Over 1,400 review articles on exogenous CO were published by 2009, yet "this broader 21st century perspective is missing from EPA's review." Donnay at ¶138-140.

EPA, notes that the evidence of harmful effects of CO, other than effects on citizens with CAD, is "limited." *See infra* Part II; (JA __) EPA-HQ-OAR-2008-0015-0187(54299). However, the largest limitation on EPA's evidence is its own failure to consider recent studies on harmful effects of CO. EPA chose to base its final NAAQS on six clinical studies over 20 years old that use COHb as the measure of CO exposure, and ignored recent epidemiological, CO poisoning and review studies that refute this contention.

B. EPA failed to explain its continued reliance on older clinical studies.

The Supreme Court has held that EPA's statutory requirement to set a NAAQS based on the "latest scientific knowledge" is a limitation on the agency's authority. *Whitman v. Am. Trucking Ass'n*, 531 U.S. 457, 473 (2001). More recently, in *Coal. of Battery Recyclers Ass'n v. E.P.A.*, 604 F.3d 613, 616 (D.C. Cir. 2010), this Court addressed the question of whether EPA's reliance on a certain subset of studies was sufficient to meet its obligation to rely on the "latest scientific knowledge" in reviewing a NAAQS for lead. EPA considered "some 6,000 studies," when it reviewed the lead NAAQS in 2008. From these 6,000 studies EPA chose to base its decision on four specific study-groups of children

and gave a reasoned explanation for those decisions. *Id.* at 620. The petitioners in *Battery Recyclers* claimed EPA's exclusion of three groups from the same studies, constituted a failure to consider the latest scientific knowledge. *Id.* However, the Court upheld EPA's decision here because EPA made a **reasoned** choice to select groups "with blood lead levels closer to the mean blood lead level of today's population of U.S. children." *Id.*

With regard to the CO NAAQS rulemaking, EPA made no such reasoned decision to rely on older clinical studies, while excluding more recent non-clinical studies. Indeed, there is no indication in the record that EPA considered evidence that COHb is an ineffective or even counterproductive indicator of CO exposure. Instead, EPA placed "principal emphasis" on six studies that used imprecise (v)COHb measurement methods to study the effect of brief acute CO exposures. (JA __) EPA-HQ-OAR-2008-0015-0187(54300); *see also* Donnay at ¶71.

Significant evidence exists that COHb, particularly (v)COHb is not the proper means of measuring CO exposure and health effects. Donnay at ¶41-70. "The World Health Organization has recognized since 2000 'ambient CO may have even more serious health consequences than does COHb formation.'" EPA-HQ-OAR-2008-0015-0179(2). Two U.S. government agencies, the Agency for Toxic Substances and Disease Registry, and the National Research Council's Committee on Toxicology, have both recognized in recent years that CO exposure

has no identifiable threshold and adverse effects of CO are likely present at levels where COHb, is not the best indicator or measurement of effects. (JA __) EPA-HQ-2008-0015-0179(2). In its 2000 AQCD, EPA seemed to agree, stating clinical "studies conducted in the 1980's and earlier distributions of COHb levels . . . that were relied on heavily in the previous assessment are **<u>no longer relevant</u>** to the current picture of ambient CO exposure in the 1990's." (JA__) EPA-HQ-OAR-2008-0015-0052(47).

Further, EPA was confronted with testimony during its review that COHb might not be the best measure of CO exposure. *See generally*, (JA __) EPA-HQ-OAR-2008-0015-0161. Testimony clarified, the greater amount of COHb in the blood, the less CO diffuses into tissues. *Id*.(4-5). The greatest danger of tissue uptake is at lower levels, less than 25ppm. *Id*.(5). In fact, at such low levels of CO exposure, COHb rises very slowly, taking at least 17-24 hours to reach equilibrium, all the while inhaled CO remains free in the blood and "easily diffuses into tissues, but only as long as CO concentrations are lower." Donnay at ¶ 37-41. For this reason, "[c]linicians are taught not to rely on COHb and researchers no longer study it." (JA __) EPA-HQ-OAR-2008-0015-0161(6).

Others pointed out that the clinical studies relied upon by EPA improperly conflate or confuse two different forms of COHb, as the Allred study did. Donnay at ¶25-40; EPA-HQ-OAR-2008-0015-0179(2-4). Not only did EPA fail to

acknowledge the studies it relied upon use potentially problematic measures, but it discounted epidemiologic studies which could better demonstrate effects from CO at low levels of CO exposure. EPA-HQ-OAR-2008-0015-0187(54299); Donnay at ¶106-26.

EPA also ignored new types of clinical studies that use "exhaled CO" which "is a more consistent biomarker than COHb." EPA-HQ-OAR2008-0015-0179(8); Donnay at ¶65. One commenter presented 117 studies not in the ISA that correlate exhaled CO to many negative health effects. *Id*. The same commenter presented another "18 studies of other biomarkers of CO exposure besides COHb and breath CO." *Id.*

EPA based its NAAQS on studies that measure exposure and health effects with COHb levels, while barely acknowledging recent studies that show serious health effects at lower levels of exposure in which COHb is not a good indicator of exposure. *See* (JA __) EPA-HQ-OAR-2008-0015-0187(54298-302); EPA-HQ-ORD-2007-0925-0017(5-41 to 5-44). But EPA must "consider **all** relevant factors" when setting a NAAQS. *See Am. Farm Bureau Fed'n v. E.P.A.*, 559 F.3d 512, 520 (D.C. Cir. 2009). Certainly, an agency should not be allowed to base its scientific decision on information that is refuted by newer studies presented to it without reasoned explanation. *See Am. Radio Relay v. FCC*, 524 F.3d 227, 241 (D.C. Cir. 2008).

C. EPA failed to explain why it did not give more weight to the epidemiological science

EPA, as any agency engaged in a scientific review, has an obligation not to engage in "sheer guesswork." *Am. Petroleum Inst. v. Costle*, 665 F.2d 1176, 1186-87 (D.C. Cir. 1981). Instead, EPA must base its decision on "evidence of risk," and neglect of this obligation is grounds for the Court to remand EPA's decision. *Id.* This Court has made this obligation explicit to EPA—the agency must provide a rational explanation as to why it has chosen to base a NAAQS on certain scientific evidence and not other facially relevant scientific evidence. *See Am. Farm Bureau Fed'n v. E.P.A.*, 559 F.3d 512, 524 (D.C. Cir. 2009); *Am. Radio Relay v. FCC*, 524 F.3d 227, 241 (D.C. Cir. 2008).

EPA's Final Rule referenced just 17 of the 279 epidemiological studies found in the ISA. (JA__) EPA-HQ-OAR-2008-0015-0187(54321-23). But more than half of the 279 epidemiological studies referenced in the ISA report statistically significant positive associations with dozens of adverse outcomes. (JA__) EPA-HQ-OAR-2008-0015-0179(9). By failing to address these studies, EPA improperly characterized the epidemiological evidence. In the Final Rule, EPA states the epidemiological evidence on cardiac effects supports the clinical science, and therefore, retention of the current standard. EPA-HQ-OAR-2008-0015-0187(34300-01). One study EPA cites for this contention is the Bell 2009

study. *Id.* This study, which included over 9.3 million subjects nationwide, actually makes very clear the current level of CO standard is not protective of public health. *See* Donnay at ¶¶116-120 (discussing (JA__) EPA-HQ-OAR-2008-0015-0053). It reported increases in CVD mortality of approximately 1.5% for the first 1ppm of additional peak 1 hr average CO exposure and lower risk, 0.5% for exposures in the range of 2-11 ppm, which includes EPA current 1-hour standard of 9 ppm. *Id.* at ¶¶116-120.

Further, EPA cherry picked epidemiological studies to use when it suited their purposes. At one point in the Final Rule, EPA states, "[t]he epidemiological evidence has expanded considerably since the last review including numerous additional studies coherent with the . . . controlled human exposure studies of CAD patients." (JA __) EPA-HQ-OAR-2008-0015-0187(54300-01). Then later stated, "there are uncertainties associated with the epidemiological evidence that complicate the quantitative interpretation of the epidemiologic findings." *Id.*(54302).

Both the ISA and public comments contain citations to multiple studies not considered by EPA, that demonstrate health effects on the respiratory system, children, elderly, asthmatics, pregnant women, fetuses and neonates, and many more. (JA__) EPA-HQ-ORD-2007-0925-0017(5-114 to 5-124); Donnay at ¶114,127,133,142. For each of these categories the ISA states the epidemiological

evidence is "suggestive of a causal relationship," but EPA disregarded this scientific evidence when setting the final NAAQS. (JA__) EPA-HQ-OAR-2008-0015-0187(54306).

Commenters and CASAC also argued the epidemiological evidence should be given more consideration. CASAC encouraged EPA to place "greater emphasis on the findings of the epidemiologic studies." (JA __) EPA-HQ-OAR-2008-0015-0029(2). Further, ALA alone cited 11 epidemiological studies that found harmful effects on lung health due to CO exposure at current ambient levels. (JA __) EPA-HQ-OAR-2008-0015-0181(8).

In the ISA, EPA stated evidence of CO's effect on respiratory morbidity was "suggestive of a causal relationship." EPA-HQ-ORD-2007-0925-0017(62). Yet in the final rule EPA dismisses the epidemiological evidence as "uncertain" and "limited." EPA-HQ-2008-0015-0187. EPA cannot simply dismiss this information with short phrases and cursory explanation. By doing so, EPA failed to comply with its statutory obligations "to consider important aspects of the problem." *Motor Vehicles Manufacturers Assoc. v. State Farm Mutual*, 463 U.S. 29, 43 (1983).

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II. EPA failed to meet its statutory obligations to protect public health with an adequate margin of safety.

A. The current CO NAAQS does not protect *all* susceptible populations, including fetuses, children, the elderly, diabetics, and the anemic.

EPA did not consider whether the current standard protects all susceptible populations. *See American Lung*, 134 F.3d at 389. Sensitive, susceptible, or vulnerable are terms used in "identifying population groups or life stages at relatively higher risk for health risk from a specific pollutant." EPA-HQ-OAR-2008-0015-0187(54299); *see also American Lung*, 134 F.3d at 389 (noting sensitive citizens are people with "conditions rendering them particularly vulnerable to air pollution"). EPA must set NAAQS "at a level at which there is 'an absence of adverse effect' on these sensitive individuals." *Lead Ind.*, 647 F.2d at 1153 (citation omitted).

Here, EPA has identified people with CAD as "the best-characterized population at risk of adverse CO-induced effects." EPA-HQ-OAR-2008-0015-0187(54299). But the clinical studies relied upon by EPA **analyzed only the effects on adult males with CAD**. *See* (JA __) EPA-HQ-OAR-2008-0015-0039(1); (JA __) EPA-HQ-OAR-2008-0015-0041(1); (JA __) EPA-HQ-OAR-2008-0015-0043(1). EPA did not adequately consider other studies regarding CO effects on other susceptible populations—such as the elderly, diabetics, the anemic,

fetuses, infants, and children. *See* Donnay at ¶106-11, Table 3; (JA __) EPA-HQ-OAR-2008-0015-0179(7, 9 & 57).

Remarkably, EPA did acknowledge that there are other susceptible populations in its Final Rule, but did not address how the current standard protects these populations:

> Those with other pre-existing diseases that may already have limited oxygen availability, increased COHb levels or increased endogenous CO production, such as people with obstructive lung diseases, diabetes and anemia; older adults; fetuses during critical phases of development and young infants or newborns; those who spend a substantial time on or near heavily traveled roadways; visitors to high-altitude locations; and people ingesting medications and other substances that enhance endogenous or metabolic CO formation.

EPA-HQ-OAR-2008-0015-0187(54299).

The administrative record in this case actually makes it clear the existing CO standard does not adequately protect other susceptible populations. The ISA, for example, states that "the controlled human exposure, epidemiologic, and toxicological studies evaluated in this assessment provide evidence for increased susceptibility among multiple subpopulations." (JA __) EPA-HQ-OAR-2008-0925-0017(69). Despite EPA's contention that information is limited, the ISA states with certainty that some of these populations are more susceptible. The ISA continues by explaining that "[d]iabetics are known to have elevated exhaled CO concentrations indicative of increased endogenous CO production rates." *Id.*(67).

The ISA also explains that anemic individuals "may be more susceptible to health effects due to ambient CO exposure" due to their elevated baseline COHb and details age as a factor determining susceptibility. *Id.*(68). The ISA further details why fetuses must also be considered a susceptible subpopulation. *Id.* ("[F]etal COHb concentrations are up to 10-15% higher on a relative basis than maternal COHb levels, and these levels are maintained over a longer period since the half-life for fetal COHb is approximately twice that of maternal COHb;" "Epidemiologic studies provide some evidence that CO exposure during pregnancy is associated with changes in birth outcomes, including PTB, cardiac birth defects, reductions in birth weight, and infant mortality in the post neonatal period;" "[E]vidence suggests that critical developmental phases may be characterized by enhanced sensitivity to CO exposure."). Even the study relied upon most heavily by EPA, the Allred study, notes that several susceptible populations exist. EPA-HQ-OAR-2008-0015-0041(2) (stating that low doses of CO can cause adverse effects in people at "high altitude, where ambient oxygen tension is reduced; anemia, where the oxygen-carrying capacity of the blood is decreased; chronic lung disease, where gas-exchange abnormalities cause hypoxemia; and occlusive vascular disease").

CASAC noted that EPA's "narrowly-defined and poorly-estimated adult CAD [focus] . . . ignores concern for many different outcomes including impacts

on fetuses and children or on the elderly." (JA __) EPA-HQ-OAR-2008-0015-0035(14); EPA-HQ-OAD-2007-0925-0019(11) ("In addition to people with cardiovascular disease there are other large population groups potentially at-risk from CO exposure."); *id.* (discussing a policy assessment citing to several epidemiological and toxicological studies supporting other susceptible populations). One CASAC member said, "we have large numbers of individuals which haven't really been tallied that are more susceptible possibly than people with coronary artery disease." (JA __) EPA-HQ-OAR-2008-0015-0019(10). CASAC also suggested more consideration of susceptible populations, including "those with pulmonary disease and the fetus." (JA __) EPA-HQ-OAR-2008-0015-0034(2).

Commenters strongly urged EPA to more fully consider whether the current standard is adequate to protect susceptible populations. ALA detailed many susceptible populations and studies supporting their increases susceptibility. (JA __) EPA-HQ-OAR-2008-0015-0181(6). Physicians for Social Responsibility submitted a comment discussing susceptible populations such as fetuses, neonates, and children. (JA __) EPA-HQ-OAR-2008-0015-0177(8). Risks to those groups include birth defects, low birth weights, increased respiratory mortality, and asthma. *Id.* Commenters rely on a number of studies in the record to support their assertions. *See generally,* (JA __) EPA-HQ-OAR-2008-0015-0207; EPA-HQ-

OAR-2008-0015-0206; Maisonet et. al., *Relation Between Ambient Air Pollution and Low Birth Weight in the Northeastern United States*, 1093 Environmental Health Persp., 351-356 (2001) (cited at (JA __) EPA-HQ-OAD-2007-0925-0017(357)); Conceicao et. al., *Air Pollution and Child Mortality: A Time-Series Study in Sao Paulo, Brazil*, 1093 Environmental Health Persp., 347-350 (2001) (cited at (JA __) EPA-HQ-ORD-2007-0925-0017(546)).

American Farm is particularly relevant to understanding EPA's failure in this case. In *American Farm*, EPA's final rule was deemed arbitrary and capricious because of EPA's failure to "explain how the annual standard it set would protect 'not only average healthy individuals, but also sensitive citizens." *American Farm*, 559 F.3d at 524. The Court held the final rule lacked "any indication of how the standard will adequately reduce risks to [susceptible populations] . . . despite (a) EPA's determination in its proposed rule that those subpopulations are at greater risk from exposure to fine particles and (b) the evidence in the record supporting that determination." *Id.* at 526.

In the case at hand, EPA's failure is the same. EPA noted in the final rule that a number of populations were at greater risk of negative health effects from CO exposure and the record supports the susceptibility of those populations. EPA-HQ-OAR-2008-0015-0187(54299). However, EPA dismisses these susceptible populations in one sentence, asserting that "information characterizing

susceptibility for these groups is limited." *Id.* In its Final Rule, EPA stated that "information is lacking on specific CO exposures" and "the nature of those effects." *Id.* EPA, however, must explain how other susceptible populations are protected, even if only limited information exists in the record.

In short, EPA's exclusive focus on clinical studies analyzing effects on adult men with CAD does not establish that the current standard protects other known, susceptible populations. *See Am. Farm*, 559 F.3d at 525 (in light of increased susceptibility among children, the court stated: "We [] doubt whether the studies of adult mortality upon which the EPA relied provide the necessary confidence concerning the risk of morbidity in children."). Because those populations are not accounted for in studies of adult men, EPA did not show a rational connection between the studies used and its decision to maintain the current CO standard.

B. The current CO NAAQS does not even protect all people with CVD, including CAD, a populations which EPA classifies as susceptible.

EPA also acknowledged that people with cardiovascular disease ("CVD") in general are also at-risk of health effects from CO exposure, but failed to consider whether the current CO NAAQS adequately protected these individuals. (JA ___) EPA-HQ-OAR-2008-0015-187. Instead, EPA only considered one susceptible population in setting the standard—those with CAD. This population, however, constitutes only a subset of those with CVD. *Id.* CVD also includes those that

suffer from "heart disease, cerebrovascular disease (e.g. stroke), hypertension (high blood pressure), and peripheral vascular diseases." *Id*. Numerous epidemiological and CO poisoning studies not fully considered by EPA, along with CASAC commentary, demonstrate that a lower standard is necessary to protect those with other forms of CVD.

First, studies cited in the record support the need for a lower standard in order to protect those with CVD. Epidemiological studies consistently offer evidence that a lower CO standard is necessary to protect those with CVD. An epidemiological study published by the American Heart Association (referred to as the "Bell study") concluded that there is "evidence of an association between short-term exposure to ambient CO and risk of CVD hospitalizations, even at levels well below the current US health-based regulatory standards." (JA __) EPA-HQ-OAR-2008-0015-0053(2). It concluded that "[t]his evidence indicates that exposure to **current CO levels may still pose a public health threat, particularly for persons with CVD**." *Id.* (emphasis added). This study found its results showing adverse effects on cardiac function to be consistent with clinical and animal studies. *Id.*(6). The Bell study found an "unexpectedly strong effect observed at current ambient levels." *Id.*

This study also notes that clinical CO studies using volunteers and an exercise protocol "may have underestimated potential susceptibility of persons

with coronary heart disease." *Id.* As little as a 1 ppm increase could change COHb between 0.1 and 0.2%. *Id.* It concluded, exposure to ambient CO "may present a far larger health burden than suspected previously." *Id.*(7).

Other epidemiological studies in the record also support the need for a lower standard in order to protect those with CVD. One study noted that in "the past 15 years, epidemiologic studies have consistently demonstrated an association between ambient levels of ambient air pollutants and daily cardiovascular mortality" and that "**[a]ssociations often have been observed at levels below the National Ambient Air Quality Standards**." (JA __) EPA-HQ-OAR-2008-0015-0058(1) (specifying with CO exposure, a 1ppm increase in an 8 hour average exposure was associated with a 3.60% increase in daily hospitalizations for certain cardiovascular effects) (emphasis added). That study concluded that CO was associated with hospital admissions at "concentrations **well below NAAQS**." *Id.*(4) (emphasis added). Another study analyzing air pollution and hospital admissions in Los Angeles, noted that "a low range of . . . CO does not necessarily rule out an effect of CO on cardiovascular morbidity." (JA __) EPA-HQ-OAR-2008-0015-0057(8). That study discussed how CO concentrations near highways and areas of heavy traffic, like those lived in by Petitioners, "exceed background levels and may cause appreciable cardiovascular stress." *Id.* That study also found "increased cardiovascular effects" on people over the age of 65 and diabetics. *Id.*

One CASAC panelist plainly stated that "there is indeed a risk for a variety of cardiovascular decompensations to arise from ambient CO in the range of only several parts per million." (JA __) EPA-HQ-OAR-2008-0015-0019(37). CASAC also found that if EPA gave epidemiological studies more weight, such as those described above, EPA would find that "health effects are occurring at levels below the current standard," thus supporting a "tightening of the current standard." (JA __) EPA-HQ-OAR-2008-0015-0029(12).

Second, CASAC repeatedly recommended that EPA look at CVD as a whole, rather than the subset of those with CAD. The panel as a whole agreed that "the discussion of vulnerable subpopulation is focused too narrowly on [CAD]." (JA __) EPA-HQ-ORD-2008-0925-0019(13). CASAC noted "EPA's singular focus on CAD will underestimate the at-risk population." *Id.*(12). "A large at-risk population includes people with CVD who have not yet been formally diagnosed with [CAD]." *Id.* For example, stroke would be covered by CVD as a category, but it is not included in CAD. *Id.* This is problematic because there is an association between stroke and small ambient CO increases. *Id.* Thus, many people falling into the broader category of CVD are not protected by a standard that focuses directly on CAD.

Overall, the record supports the need for a lower standard in order to protect those with CAD, and more broadly CVD. Because EPA's final rule is contrary to

and not supported by the evidence in the record, this Court should find its rule arbitrary and capricious.

C. The current CO NAAQS does not protect public health from effects other than cardiovascular effects.

Finally, EPA further ignored known health effects from CO exposure other than CVD, including: central nervous system effects, birth outcomes, developmental effects, respiratory morbidity, and mortality. *See* EPA-HQ-OAR-2008-0015-0187(54299); *see also* Donnay at ¶¶106-11. EPA did not address the evidence supporting these other health effects, rather stated only that the evidence was 'only limited.' EPA-HQ-OAR-2008-0015-0187(54299).

Studies cited in the administrative record suggest that the evidence as to these other health effects is far less "limited" than EPA asserts. The ISA alone points to numerous studies looking at preterm birth, birth defects, fetal growth, and infant mortality. (JA __) EPA-HQ-ORD-2007-0925-0017(64). Epidemiological studies from California "reported consistent positive associations with CO exposure during early pregnancy when exposures were assigned from monitors within close proximity of the mother's residential address." *Id.* More studies provide support for an association between CO and preterm birth. *Id.*(64-65). Two studies showed a positive association between CO exposure and cardiac birth defects. *Id.* Further, "[t]here is evidence of ambient CO exposure during pregnancy having a negative effect on fetal growth in epidemiologic studies."

Id.(64). The ISA also acknowledges a "positive associations between short-term exposure to CO and respiratory-related outcomes including pulmonary function, respiratory symptoms, medication use, hospital admissions, and ED visits." *Id.*(65). While the ISA concludes that, other than cardiovascular effects, health effects of CO are only supported by a "suggestive" relationship, the evidence indicates a correlation strong enough to warrant at least an explanation in the final rule. EPA did not reference any evidence in the final rule demonstrating a positive correlation between CO exposure and these other health effects.

Evidence of other health effects is prevalent throughout other portions of the record as well. CASAC was also concerned about other health effects. The panel recommended that "a broad set of health outcomes be considered, beyond cardiac ischemia." (JA __) EPA-HQ-OAR-2008-0015-0034(2). A Toronto study showed a strong association between one-hour CO exposure at and below 6 ppm and hospital admissions for asthma, acute bronchitis, croup, and pneumonia for children. Burnett M., et. al., *Association Between Ozone and Hospitalization for Acute Respiratory Diseases in Children Less than 2 Years of Age*, 153 Am. J. Epidemiol. 444-452 (2001) (cited at (JA __) EPA-HQ-OAR-2008-0015-0181(16) and EPA-HQ-ORD-2007-0925-0017(347). Another study found similar results at a 24-hour average of less than 5 ppm. Yang Q., et. al., *Association Between Ozone and Respiratory Admissions Among Children and the Elderly in Vancouver,*

Canada, 15 Inhal. Toxicol. 1297-1308 (2003) (cited at (JA __) EPA-HQ-OAR-2008-0015-0181(18)). Studies repeatedly showed negative respiratory health effects on children with asthma. Lin M., et. al., *Gaseous Air Pollutants and Asthma Hospitalization of Children with Low Household Income in Vancouver, British Columbia, Canada*, Am. J. Epidemiol. 159: 294-303 (2004) (cited at (JA __) EPA-HQ-OAR-2008-0015-0181(17)); Slaughter J.C., et. al., *Association Between Particulate Matter and Emergency Room Visits, Hospital Admissions, and Mortality in Spokane, Washington*, 15 J. Expo. Sci. Environ. Epidemiol. 153-159 (2005) (cited at (JA __) EPA-HQ-OAR-2008-0015-0181(18)); Peel J.L., et. al., *Ambient Air Pollution and Respiratory Emergency Department Visits*, 16 Epidemiology 164-174 (2005) (cited at (JA __) EPA-HQ-OAR-2008-0015-0181(18)). Low-level exposure to CO showed respiratory effects in the elderly as well. Yang Q., et. al., *Association Between Ozone and Respiratory Admissions Among Children and the Elderly in Vancouver, Canada*, 15 Inhal. Toxicol., 1297-1308 (2003) (cited at (JA __) EPA-HQ-OAR-2008-0015-0181(18)). In fact, the comment provided by ALA cites to many studies all analyzing effects of CO well below the current standard. (JA __) EPA-HQ-OAR-2008-0015-0181.

In short, EPA's final rule does not address all health effects caused by CO exposure and does not explain how vulnerable populations are protected by the current standard.

III. EPA Mischaracterized and Ignored the Recommendations of the Clean Air Scientific Advisory Committee.

EPA must "set forth or summarize and provide a reference to any pertinent findings, recommendations, and comments by [CASAC], and, if the proposal differs in any important respect from any of these recommendations, an explanation of the reasons for such differences." 42 U.S.C. § 7607. Moreover, EPA must adequately explain its rejection of CASAC's recommendations. *Am. Farm*, 559 F.3d at 520, 528. Throughout the entire rulemaking process, CASAC members consistently recommended that more weight be given to epidemiological studies that contain data supporting the need for a lower standard, that the Allred study should be given less weight, and that EPA expand its analysis to in include a broader number of health outcomes. EPA's analysis of CASAC's recommendations, however, does not provide a coherent rationalization for its decision to keep the CO NAAQS the same.

In the final rule, the Administrator states that:

> [a]lthough CASAC expressed a preference for a lower standard, CASAC also indicated that the current evidence provides support for retaining the current suite of standards and CASAC's recommendations appear to recognize that their preference for a lower standard was contingent on a judgment as to the weight to be placed on the epidemiological evidence.

EPA-HQ-OAR-2008-0015-0187(54304). This statement, and other similar statements in the Final Rule, greatly mischaracterizes CASAC's

recommendations because: 1) EPA overstates CASAC's agreement with the EPA's conclusion that evidence provides support for retaining the current suite of standards; and 2) although it could be perceived that CASAC's preference for a lower standard was contingent on the weight given to the epidemiologic data, it does not reflect CASAC's repeated recommendation that the data be given more weight.

First, EPA overstates CASAC's agreement with the EPA's conclusion that the evidence supports a decision to retain current standards by overemphasizing a single CASAC comment made in passing. In making this assertion, the Administrator cites to the comment letter regarding the PA dated June 8, 2010. EPA-HQ-OAR-2008-0015-0187(54304) (*citing* EPA-HQ-OAR-2008-0015-0029(12)). This letter states that based on EPA Staff's analysis, "they conclude that the body of evidence and the quantitative exposure and dose estimates provide support for a standard at least as protective as the current standards, i.e. the data provide support for **retaining or revising** the current 8-hr standard." (JA __) EPA-HQ-OAR-2008-0015-0029(12) (emphasis added). CASAC then states that overall the Panel agrees with this conclusion, and then immediately points out that "[i]f the epidemiological evidence is given additional weight, the conclusion could be drawn that the health effects are occurring at levels below the

current standard, which would support the tightening of the current standard." *Id*. In the next paragraph, CASAC acknowledged that in indicating a range of policy options, EPA staff stated that the evidence is consistent with maintaining standards at current levels. *Id.* Immediately after noting EPA's conclusion regarding retaining the current standards, CASAC stated, "[h]owever, given new evidence, primarily epidemiological, that there are many individuals potentially at risk in addition to those with coronary artery disease . . . there is reason to consider reducing the standard below the current level(s)." *Id.* CASAC then suggested that EPA offer example policy options. *Id.*(13). The examples CASAC offered all included ranges lower than current standards. *Id.*

Second, EPA states that the CASAC's preference for a lower standard appeared to be contingent on the amount of weight given to the epidemiological studies. EPA-HQ-OAR-2008-0015-0187(54304). Even if this was a reasonable perception of CASAC's comments, it was not reasonable for EPA to use this "contingency" as an excuse to ignore CASAC's multiple recommendations that EPA give greater weight to epidemiological studies. Although some CASAC panelists felt that EPA should proceed with caution in considering epidemiologic data, the overall consensus of CASAC was that EPA should put greater emphasis in the

epidemiologic data. EPA-HQ-OAR-2008-0015-0029(2). CASAC explained that the epidemiological studies have expanded considerably since the previous CO NAAQS review ((JA __) EPA-HQ-OAR-2008-0015-0187(54300)) and epidemiologic evidence may in fact be more realistic than the controlled human exposure data (EPA-HQ-OAR-2008-0015-0029(7)). Further, because it would not be possible or ethical to do clinical studies on many populations, such as pregnant women and fetuses, reliance on clinical studies ignores many susceptible populations that Congress intended to protect with the NAAQS program. EPA-HQ-OAR-2008-0015-0029(12).

In agreeing that the data supports a decision to "retain or revise" the current 8-hour standard, CASAC hardly expresses a preference for retaining the current standards. In concluding that current standards provide sufficient protection from adverse health effects with an adequate margin of safety the Administrator gives great weight to the **one comment** in the CASAC letters that supports its conclusion, and almost no weight at all to the vast majority of comments and direct recommendations that more weight be given to the epidemiological studies.

EPA stated in the Final Rule that she dismissed CASAC's preference because she determined that the "uncertainties and limitations to be too great for the epidemiological evidence to provide a basis for revising the current standards."

EPA-HQ-OAR-2008-0015-0187(54304). While EPA notes the difficulties in analyzing this data, it does not adequately explain why it is not following CASAC's recommendation to give weight to these studies regardless of the difficulties. Given the amount of uncertainty inherent in all scientific studies, and especially considering the great weight given to the Allred study, which has its own unique set of problems, EPA's reasons for dismissing CASAC's recommendations amount to mere assertions. Such assertions do not provide a sufficient rational basis for agency decision making. *See Cement Kiln Recycling Coal. v. EPA*, 255 F.3d 855, 866 (D.C. Cir. 2001) (agency must support decisions with "substantial evidence—not mere assertions"). This Court has repeatedly indicated that the precautionary nature of the CAA does not mandate certainty before EPA must act to protect health. *See Lead Industries*, 647 F.2d at 1155. Rather, EPA must act as soon as there is any data suggesting health effects from a pollutant. *See id.* (citing *Ethyl Corp. v. EPA*, 541 F.2d 1, 24-25 (D.C. Cir. 1976) ("reasonable medical concerns" and theory long precede certainty. Yet the statutes and common sense demand regulatory action to prevent harm, even if the regulator is less than certain that harm is otherwise inevitable.).

Further, EPA acknowledged that "CASAC expressed a preference for a lower standard." EPA-HQ-OAR-2008-0015-0187(54304). However, nowhere in the final rule does EPA actually discuss what a lower standard might look like or

why it would not provide better protection of the general public and susceptible populations.

Because EPA vastly mischaracterized CASAC's recommendations, it failed to adequately respond to and analyze the input received from CASAC. In doing so, EPA failed to consider relevant factors and provide a rational explanation for its actions. Therefore, EPA was arbitrary and capricious in its decision not to revise the CO NAAQS.

IV. EPA violated the CAA when it failed to set a secondary standard for CO.

Congressional concern about the causes and effects of climate change is nothing new. *See Mass. v. E.P.A.*, 549 U.S. 497, 506-09 (2007) (providing a brief history of federal legislative efforts to reduce and reverse effects of manmade pollution on climate). From the National Climate Program Act of 1978—established to "assist the Nation and the World" to understand and respond to natural and man-induced climate process and their implication"—to the Global Climate Protection Act of 1987, to the CAA provisions at issue in this case, Congress has made consistent and concerted efforts to insure that 'global warming' remains a relevant consideration as the federal government constantly re-evaluates environmental policy. *See id.* This legislative history gives critical context to any discussion of the breadth of secondary NAAQS protections of public welfare, 42 U.S.C. § 7409(b), because it indicates that a proper reading of these statutory

provisions must account for the broad history of congressional concern about climate change.

The breadth of these protections only becomes clearer in considering the statutory language of the CAA. EPA is required to establish secondary standards that sufficiently protect public welfare from "**any known or anticipated** adverse effects." *Id.* (emphasis added). The broad scope of this protection is evident when considering, for example, that Congress could have required the EPA to establish secondary NAAQS only to protect against "some," "limited," or "certain enumerated" adverse effects. Instead, Congress chose to fortify this requirement with all-inclusive protection against "any" adverse effects. *Id.* Thus, Congress carefully selected language that protects public welfare to the broadest extent possible.

Consider also the protections against both **known** and **anticipated** adverse effects on public welfare. *Id.* This highlights congressional intent to protect public welfare both from harm already done, and from potential harm that can still be avoided or mitigated. Noting these broad prescriptive protections, this Court has held that EPA must establish secondary standards "as soon as it can anticipate adverse effects . . . [and] as soon as it has enough information **(even if crude)** to 'anticipate' such effects." *Am. Trucking Ass'n, Inc. v. EPA*, 283 F.3d 355, 380 (D.C. Cir. 2002) (emphasis added).

Furthermore, Congress's definition of public welfare itself adds to the breadth of secondary NAAQS protections. That definition includes "effects on soils, water, crops, vegetation, man-made materials, animals, wildlife, weather, visibility, [and] **climate** . . . " 42 U.S.C. §7602 (emphasis added); *see also Nat'l Lime Ass'n v. E.P.A.*, 627 F.2d 416 (holding that Congress intended the definition of public welfare to be even more expansive than the specifically enumerated effects).

Here, EPA failed to live up to this mandate because: (1) the administrative record shows that EPA's own experts believed the levels of CO in the ambient air adversely affect climate—which is to say they adversely affect public welfare—and this alone should have compelled EPA to establish a secondary CO NAAQS; and (2) to the extent the evidence behind that conclusion is inconclusive or dependent upon co-pollutant analysis, EPA failed to provide the required "adequate margin of safety," 42 U.S.C. §7409(b) and improperly allowed a lack of total certainty to influence its decision. *Am. Trucking*, 283 F.3d at 380.

EPA knows that the levels of CO in ambient air adversely affect public welfare. *See e.g.*, (JA __) EPA-HQ-ORD-2007-0925-0013(92) ("The evidence that [CO] has an adverse impact on climate in the oxidizing capacity of the atmosphere is strong."); *id.*(94)("[W]e know that the atmospheric concentration of carbon monoxide, like carbon dioxide, is too high to protect people from adverse

impacts of climate change."); (JA __) EPA-HQ-ORD-2007-0925-0017 ("a causal relationship exists between current atmospheric concentrations of CO and effects on climate."); (JA __) EPA-HQ-ORD-2007-0925-0019(27) (CO "is both a local pollutant and a contributor to climate change); *id*. ("the current ambient concentration-based standards are not appropriate for large-scale global atmospheric concentration concerns aimed at protecting welfare"). One CASAC member even stated "the evidence all points to the need for new regulations for the climate effects of CO. The current ambient concentration-based standards are not appropriate for large-scale global atmospheric concentration concerns aimed at protecting welfare." (JA__) EPA-HQ-ORD-2007-0925-0019(27). Furthermore, CASAC candidly advised EPA that "CO is low hanging fruit with respect to short term (20-year) climate forcing. (JA__) EPA-HQ-OAR-2008-0015-0025.

Unfortunately, EPA did not take this advice though it plainly acknowledged that "**<u>CO is classified as a short-lived climate forcing agent</u>**, prompting CO emission reductions to be considered as a possible strategy to mitigate effects of global warming." (JA __) EPA-HQ-OAR-2008-0015-0025(114) (emphasis added). In the first draft of the ISA, EPA goes on to describe some concerns with the precise evaluation of CO's effect on climate change; but those concerns do nothing to negate EPA's own conclusion that CO is a climate forcing agent.

Here, once again, attention to specifics of the statutory language is required. The CAA does not call for secondary NAAQS only when the effect of a criteria pollutant is completely certain—rather it calls for secondary NAAQS based on any "anticipated" adverse effect. 42 U.S.C. § 7409(b). Therefore, if CO is already classified as a climate forcing agent (i.e. causes climate change), then it adversely affects public welfare, and EPA must establish a secondary NAAQS.

This conclusion is compelled by the statutory requirement that secondary NAAQS must provide an "adequate margin of safety." 42 U.S.C. 7409(b).

CONCLUSION

For the foregoing reasons, Petitioners respectfully request this Court grant the Petition, vacate the Final Rule, Review of National Ambient Air Quality Standards for Carbon Monoxide, 76 Fed. Reg. 54294 (August 31, 2011).

Dated this 14th day of May, 2012 (corrected version).

Respectfully submitted,

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CERTIFICATE OF COMPLIANCE

As required by Fed. R. App. P. 32(a)(7)(c), I certify that this brief is proportionally spaced and contains 13,408 words. I relied on my word processor to obtain the count and it is Microsoft Office 2007. I certify that the information on this form is true and correct to the best of my knowledge and belief formed after a reasonable inquiry.

Dated this 14th day of May, 2012.

Respectfully submitted,

s/ Michael Ray Harris

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CERTIFICATE OF DIGITAL SUBMISSIONS

I hereby certify that a copy of the foregoing **Petitioner's Brief**, as submitted in Digital Form, is an exact copy of the written document filed with the Clerk and has been scanned for viruses with Symantec Antivirus; Version 10.11.0.5002.33; last updated on May 14, 2012, and, according to the program, is free of viruses.

Dated this 14th day of May, 2012.

Respectfully submitted,

s/ Michael Ray Harris

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Addendum A

grants shall be made under this section until the Administrator has consulted with the appropriate official as designated by the Governor or Governors of the State or States affected.

(d) The Administrator, with the concurrence of any recipient of a grant under this section may reduce the payments to such recipient by the amount of the pay, allowances, traveling expenses, and any other costs in connection with the detail of any officer or employee to the recipient under section 301 of the Act, when such detail is for the convenience of, and at the request of, such recipient and for the purpose of carrying out the provisions of this Act. The amount by which such payments have been reduced shall be available for payment of such costs by the Administrator, but shall, for the purpose of determining the amount of any grant to a recipient under subsection (a) of this section, be deemed to have been paid to such agency.

(e) No application by a State for a grant under this section may be disapproved by the Administrator without prior notice and opportunity for a public hearing in the affected State, and no commitment or obligation of any funds under any such grant may be revoked or reduced without prior notice and opportunity for a public hearing in the affected State (or in one of the affected States if more than one State is affected).

[42 U.S.C. 7405]

INTERSTATE AIR QUALITY AGENCIES OR COMMISSIONS

SEC. 106. For the purpose of developing implementation plans for any interstate air quality control region designated pursuant to section 107 or of implementing section 176A (relating to control of interstate air pollution) or section 184 (relating to control of interstate ozone pollution), the Administrator is authorized to pay, for two years, up to 100 per centum of the air quality planning program costs of any commission established under section 176A (relating to control of interstate air pollution) or section 184 (relating to control of interstate ozone pollution) or any agency designated by the Governors of the affected States, which agency shall be capable of recommending to the Governors plans for implementation of national primary and secondary ambient air quality standards and shall include representation from the States and appropriate political subdivisions within the air quality control region. After the initial two-year period the Administrator is authorized to make grants to such agency or such commission in an amount up to three-fifths of the air quality implementation program costs of[1] such agency or commission.

[42 U.S.C. 7406]

AIR QUALITY CONTROL REGIONS

SEC. 107. (a) Each State shall have the primary responsibility for assuring air quality within the entire geographic area comprising such State by submitting an implementation plan for such

[1] Section 102(f)(2) of Public Law 101–549 inserted "any commission established under section 176A (relating to control of interstate air pollution) or section 184 (relating to control of ozone pollution)" after "program costs of" in section 106. The amendment was probably intended to insert this language only in the first place these words appear.

State which will specify the manner in which national primary and secondary ambient air quality standards will be achieved and maintained within each air quality control region in such State.

(b) For purposes of developing and carrying out implementation plans under section 110—

(1) an air quality control region designated under this section before the date of enactment of the Clean Air Amendments of 1970, or a region designated after such date under subsection (c), shall be an air quality control region; and

(2) the portion of such State which is not part of any such designated region shall be an air quality control region, but such portion may be subdivided by the State into two or more air quality control regions with the approval of the Administrator.

(c) The Administrator shall, within 90 days after the date of enactment of the Clean Air Amendments of 1970, after consultation with appropriate State and local authorities, designate as an air quality control region any interstate area or major intrastate area which he deems necessary or appropriate for the attainment and maintenance of ambient air quality standards. The Administrator shall immediately notify the Governors of the affected States of any designation made under this subsection.

(d) DESIGNATIONS.—

(1) DESIGNATIONS GENERALLY.—

(A) SUBMISSION BY GOVERNORS OF INITIAL DESIGNATIONS FOLLOWING PROMULGATION OF NEW OR REVISED STANDARDS.—By such date as the Administrator may reasonably require, but not later than 1 year after promulgation of a new or revised national ambient air quality standard for any pollutant under section 109, the Governor of each State shall (and at any other time the Governor of a State deems appropriate the Governor may) submit to the Administrator a list of all areas (or portions thereof) in the State, designating as—

(i) nonattainment, any area that does not meet (or that contributes to ambient air quality in a nearby area that does not meet) the national primary or secondary ambient air quality standard for the pollutant,

(ii) attainment, any area (other than an area identified in clause (i)) that meets the national primary or secondary ambient air quality standard for the pollutant, or

(iii) unclassifiable, any area that cannot be classified on the basis of available information as meeting or not meeting the national primary or secondary ambient air quality standard for the pollutant.

The Administrator may not require the Governor to submit the required list sooner than 120 days after promulgating a new or revised national ambient air quality standard.

(B) PROMULGATION BY EPA OF DESIGNATIONS.—(i) Upon promulgation or revision of a national ambient air quality standard, the Administrator shall promulgate the designations of all areas (or portions thereof) submitted under

subparagraph (A) as expeditiously as practicable, but in no case later than 2 years from the date of promulgation of the new or revised national ambient air quality standard. Such period may be extended for up to one year in the event the Administrator has insufficient information to promulgate the designations.

(ii) In making the promulgations required under clause (i), the Administrator may make such modifications as the Administrator deems necessary to the designations of the areas (or portions thereof) submitted under subparagraph (A) (including to the boundaries of such areas or portions thereof). Whenever the Administrator intends to make a modification, the Administrator shall notify the State and provide such State with an opportunity to demonstrate why any proposed modification is inappropriate. The Administrator shall give such notification no later than 120 days before the date the Administrator promulgates the designation, including any modification thereto. If the Governor fails to submit the list in whole or in part, as required under subparagraph (A), the Administrator shall promulgate the designation that the Administrator deems appropriate for any area (or portion thereof) not designated by the State.

(iii) If the Governor of any State, on the Governor's own motion, under subparagraph (A), submits a list of areas (or portions thereof) in the State designated as nonattainment, attainment, or unclassifiable, the Administrator shall act on such designations in accordance with the procedures under paragraph (3) (relating to redesignation).

(iv) A designation for an area (or portion thereof) made pursuant to this subsection shall remain in effect until the area (or portion thereof) is redesignated pursuant to paragraph (3) or (4).

(C) DESIGNATIONS BY OPERATION OF LAW.—(i) Any area designated with respect to any air pollutant under the provisions of paragraph (1) (A), (B), or (C) of this subsection (as in effect immediately before the date of the enactment of the Clean Air Act Amendments of 1990) is designated, by operation of law, as a nonattainment area for such pollutant within the meaning of subparagraph (A)(i).

(ii) Any area designated with respect to any air pollutant under the provisions of paragraph (1)(E) (as in effect immediately before the date of the enactment of the Clean Air Act Amendments of 1990) is designated by operation of law, as an attainment area for such pollutant within the meaning of subparagraph (A)(ii).

(iii) Any area designated with respect to any air pollutant under the provisions of paragraph (1)(D) (as in effect immediately before the date of the enactment of the Clean Air Act Amendments of 1990) is designated, by operation of law, as an unclassifiable area for such pollutant within the meaning of subparagraph (A)(iii).

(2) PUBLICATION OF DESIGNATIONS AND REDESIGNATIONS.—(A) The Administrator shall publish a notice in the Federal Register promulgating any designation under paragraph (1) or (5), or announcing any designation under paragraph (4), or promulgating any redesignation under paragraph (3).

(B) Promulgation or announcement of a designation under paragraph (1), (4) or (5) shall not be subject to the provisions of sections 553 through 557 of title 5 of the United States Code (relating to notice and comment), except nothing herein shall be construed as precluding such public notice and comment whenever possible.

(3) REDESIGNATION.—(A) Subject to the requirements of subparagraph (E), and on the basis of air quality data, planning and control considerations, or any other air quality-related considerations the Administrator deems appropriate, the Administrator may at any time notify the Governor of any State that available information indicates that the designation of any area or portion of an area within the State or interstate area should be revised. In issuing such notification, which shall be public, to the Governor, the Administrator shall provide such information as the Administrator may have available explaining the basis for the notice.

(B) No later than 120 days after receiving a notification under subparagraph (A), the Governor shall submit to the Administrator such redesignation, if any, of the appropriate area (or areas) or portion thereof within the State or interstate area, as the Governor considers appropriate.

(C) No later than 120 days after the date described in subparagraph (B) (or paragraph (1)(B)(iii)), the Administrator shall promulgate the redesignation, if any, of the area or portion thereof, submitted by the Governor in accordance with subparagraph (B), making such modifications as the Administrator may deem necessary, in the same manner and under the same procedure as is applicable under clause (ii) of paragraph (1)(B), except that the phrase "60 days" shall be substituted for the phrase "120 days" in that clause. If the Governor does not submit, in accordance with subparagraph (B), a redesignation for an area (or portion thereof) identified by the Administrator under subparagraph (A), the Administrator shall promulgate such redesignation, if any, that the Administrator deems appropriate.

(D) The Governor of any State may, on the Governor's own motion, submit to the Administrator a revised designation of any area or portion thereof within the State. Within 18 months of receipt of a complete State redesignation submittal, the Administrator shall approve or deny such redesignation. The submission of a redesignation by a Governor shall not affect the effectiveness or enforceability of the applicable implementation plan for the State.

(E) The Administrator may not promulgate a redesignation of a nonattainment area (or portion thereof) to attainment unless—

(i) the Administrator determines that the area has attained the national ambient air quality standard;

(ii) the Administrator has fully approved the applicable implementation plan for the area under section 110(k);

(iii) the Administrator determines that the improvement in air quality is due to permanent and enforceable reductions in emissions resulting from implementation of the applicable implementation plan and applicable Federal air pollutant control regulations and other permanent and enforceable reductions;

(iv) the Administrator has fully approved a maintenance plan for the area as meeting the requirements of section 175A; and

(v) the State containing such area has met all requirements applicable to the area under section 110 and part D.

(F) The Administrator shall not promulgate any redesignation of any area (or portion thereof) from nonattainment to unclassifiable.

(4) NONATTAINMENT DESIGNATIONS FOR OZONE, CARBON MONOXIDE AND PARTICULATE MATTER (PM–10).—

(A) OZONE AND CARBON MONOXIDE.—(i) Within 120 days after the date of the enactment of the Clean Air Act Amendments of 1990, each Governor of each State shall submit to the Administrator a list that designates, affirms or reaffirms the designation of, or redesignates (as the case may be), all areas (or portions thereof) of the Governor's State as attainment, nonattainment, or unclassifiable with respect to the national ambient air quality standards for ozone and carbon monoxide.

(ii) No later than 120 days after the date the Governor is required to submit the list of areas (or portions thereof) required under clause (i) of this subparagraph, the Administrator shall promulgate such designations, making such modifications as the Administrator may deem necessary, in the same manner, and under the same procedure, as is applicable under clause (ii) of paragraph (1)(B), except that the phrase "60 days" shall be substituted for the phrase "120 days" in that clause. If the Governor does not submit, in accordance with clause (i) of this subparagraph, a designation for an area (or portion thereof), the Administrator shall promulgate the designation that the Administrator deems appropriate.

(iii) No nonattainment area may be redesignated as an attainment area under this subparagraph.

(iv) Notwithstanding paragraph (1)(C)(ii) of this subsection, if an ozone or carbon monoxide nonattainment area located within a metropolitan statistical area or consolidated metropolitan statistical area (as established by the Bureau of the Census) is classified under part D of this title as a Serious, Severe, or Extreme Area, the boundaries of such area are hereby revised (on the date 45 days after such classification) by operation of law to include the entire metropolitan statistical area or consolidated metropolitan statistical area, as the case may be, unless within such 45-day period the Governor (in consultation with State and local air pollution control agencies) notifies the Adminis-

trator that additional time is necessary to evaluate the application of clause (v). Whenever a Governor has submitted such a notice to the Administrator, such boundary revision shall occur on the later of the date 8 months after such classification or 14 months after the date of the enactment of the Clean Air Act Amendments of 1990 unless the Governor makes the finding referred to in clause (v), and the Administrator concurs in such finding, within such period. Except as otherwise provided in this paragraph, a boundary revision under this clause or clause (v) shall apply for purposes of any State implementation plan revision required to be submitted after the date of the enactment of the Clean Air Act Amendments of 1990.

(v) Whenever the Governor of a State has submitted a notice under clause (iv), the Governor, in consultation with State and local air pollution control agencies, shall undertake a study to evaluate whether the entire metropolitan statistical area or consolidated metropolitan statistical area should be included within the nonattainment area. Whenever a Governor finds and demonstrates to the satisfaction of the Administrator, and the Administrator concurs in such finding, that with respect to a portion of a metropolitan statistical area or consolidated metropolitan statistical area, sources in the portion do not contribute significantly to violation of the national ambient air quality standard, the Administrator shall approve the Governor's request to exclude such portion from the nonattainment area. In making such finding, the Governor and the Administrator shall consider factors such as population density, traffic congestion, commercial development, industrial development, meteorological conditions, and pollution transport.

(B) PM–10 DESIGNATIONS.—By operation of law, until redesignation by the Administrator pursuant to paragraph (3)—

(i) each area identified in 52 Federal Register 29383 (Aug. 7, 1987) as a Group I area (except to the extent that such identification was modified by the Administrator before the date of the enactment of the Clean Air Act Amendments of 1990) is designated nonattainment for PM–10;

(ii) any area containing a site for which air quality monitoring data show a violation of the national ambient air quality standard for PM–10 before January 1, 1989 (as determined under part 50, appendix K of title 40 of the Code of Federal Regulations) is hereby designated nonattainment for PM–10; and

(iii) each area not described in clause (i) or (ii) is hereby designated unclassifiable for PM–10.

Any designation for particulate matter (measured in terms of total suspended particulates) that the Administrator promulgated pursuant to this subsection (as in effect immediately before the date of the enactment of the Clean Air Act Amendments of 1990) shall remain in effect for

purposes of implementing the maximum allowable increases in concentrations of particulate matter (measured in terms of total suspended particulates) pursuant to section 163(b), until the Administrator determines that such designation is no longer necessary for that purpose.

(5) DESIGNATIONS FOR LEAD.—The Administrator may, in the Administrator's discretion at any time the Administrator deems appropriate, require a State to designate areas (or portions thereof) with respect to the national ambient air quality standard for lead in effect as of the date of the enactment of the Clean Air Act Amendments of 1990, in accordance with the procedures under subparagraphs (A) and (B) of paragraph (1), except that in applying subparagraph (B)(i) of paragraph (1) the phrase "2 years from the date of promulgation of the new or revised national ambient air quality standard" shall be replaced by the phrase "1 year from the date the Administrator notifies the State of the requirement to designate areas with respect to the standard for lead".

(6) DESIGNATIONS.—

(A) SUBMISSION.—Notwithstanding any other provision of law, not later than February 15, 2004, the Governor of each State shall submit designations referred to in paragraph (1) for the July 1997 $PM_{2.5}$ national ambient air quality standards for each area within the State, based on air quality monitoring data collected in accordance with any applicable Federal reference methods for the relevant areas.

(B) PROMULGATION.—Notwithstanding any other provision of law, not later than December 31, 2004, the Administrator shall, consistent with paragraph (1), promulgate the designations referred to in subparagraph (A) for each area of each State for the July 1997 $PM_{2.5}$ national ambient air quality standards.

(7) IMPLEMENTATION PLAN FOR REGIONAL HAZE.—

(A) IN GENERAL.—Notwithstanding any other provision of law, not later than 3 years after the date on which the Administrator promulgates the designations referred to in paragraph (6)(B) for a State, the State shall submit, for the entire State, the State implementation plan revisions to meet the requirements promulgated by the Administrator under section 169B(e)(1) (referred to in this paragraph as "regional haze requirements").

(B) NO PRECLUSION OF OTHER PROVISIONS.—Nothing in this paragraph precludes the implementation of the agreements and recommendations stemming from the Grand Canyon Visibility Transport Commission Report dated June 1996, including the submission of State implementation plan revisions by the States of Arizona, California, Colorado, Idaho, Nevada, New Mexico, Oregon, Utah, or Wyoming by December 31, 2003, for implementation of regional haze requirements applicable to those States.

(e)(1) Except as otherwise provided in paragraph (2), the Governor of each State is authorized, with the approval of the Administrator, to redesignate from time to time the air quality control re-

gions within such State for purposes of efficient and effective air quality management. Upon such redesignation, the list under subsection (d) shall be modified accordingly.

(2) In the case of an air quality control region in a State, or part of such region, which the Administrator finds may significantly affect air pollution concentrations in another State, the Governor of the State in which such region, or part of a region, is located may redesignate from time to time the boundaries of so much of such air quality control region as is located within such State only with the approval of the Administrator and with the consent of all Governors of all States which the Administrator determines may be significantly affected.

(3) No compliance date extension granted under section 113(d)(5) (relating to coal conversion) shall cease to be effective by reason of the regional limitation provided in section 113(d)(5) if the violation of such limitation is due solely to a redesignation of a region under this subsection.

[42 U.S.C. 7407]

AIR QUALITY CRITERIA AND CONTROL TECHNIQUES

SEC. 108. (a)(1) For the purpose of establishing national primary and secondary ambient air quality standards, the Administrator shall within 30 days after the date of enactment of the Clean Air Amendments of 1970 publish, and shall from time to time thereafter revise, a list which includes each air pollutant—

(A) emissions of which, in his judgment, cause or contribute to air pollution which may reasonably be anticipated to endanger public health or welfare;

(B) the presence of which in the ambient air results from numerous or diverse mobile or stationary sources; and

(C) for which air quality criteria had not been issued before the date of enactment of the Clean Air Amendments of 1970, but for which he plans to issue air quality criteria under this section.

(2) The Administrator shall issue air quality criteria for an air pollutant within 12 months after he has included such pollutant in a list under paragraph (1). Air quality criteria for an air pollutant shall accurately reflect the latest scientific knowledge useful in indicating the kind and extent of all identifiable effects on public health or welfare which may be expected from the presence of such pollutant in the ambient air, in varying quantities. The criteria for an air pollutant, to the extent practicable, shall include information on—

(A) those variable factors (including atmospheric conditions) which of themselves or in combination with other factors may alter the effects on public health or welfare of such air pollutant;

(B) the types of air pollutants which, when present in the atmosphere, may interact with such pollutant to produce an adverse effect on public health or welfare; and

(C) any known or anticipated adverse effects on welfare.

(b)(1) Simultaneously with the issuance of criteria under subsection (a), the Administrator shall, after consultation with appro-

priate advisory committees and Federal departments and agencies, issue to the States and appropriate air pollution control agencies information on air pollution control techniques, which information shall include data relating to the cost of installation and operation, energy requirements, emission reduction benefits, and environmental impact of the emission control technology. Such information shall include such data as are available on available technology and alternative methods of prevention and control of air pollution. Such information shall also include data on alternative fuels, processes, and operating methods which will result in elimination or significant reduction of emissions.

(2) In order to assist in the development of information on pollution control techniques, the Administrator may establish a standing consulting committee for each air pollutant included in a list published pursuant to subsection (a)(1), which shall be comprised of technically qualified individuals representative of State and local governments, industry, and the economic community. Each such committee shall submit, as appropriate, to the Administrator information related to that required by paragraph (1).

(c) The Administrator shall from time to time review, and, as appropriate, modify, and reissue any criteria or information on control techniques issued pursuant to this section. Not later than six months after the date of the enactment of the Clean Air Act Amendments of 1977, the Administrator shall revise and reissue criteria relating to concentrations of NO_2 over such period (not more than three hours) as he deems appropriate. Such criteria shall include a discussion of nitric and nitrous acids, nitrites, nitrates, nitrosamines, and other carcinogenic and potentially carcinogenic derivatives of oxides of nitrogen.

(d) The issuance of air quality criteria and information on air pollution control techniques shall be announced in the Federal Register and copies shall be made available to the general public.

(e) The Administrator shall, after consultation with the Secretary of Transportation, and after providing public notice and opportunity for comment, and with State and local officials, within nine months after enactment of the Clean Air Act Amendments of 1989[1] and periodically thereafter as necessary to maintain a continuous transportation-air quality planning process, update the June 1978 Transportation-Air Quality Planning Guidelines and publish guidance on the development and implementation of transportation and other measures necessary to demonstrate and maintain attainment of national ambient air quality standards. Such guidelines shall include information on—

(1) methods to identify and evaluate alternative planning and control activities;

(2) methods of reviewing plans on a regular basis as conditions change or new information is presented;

(3) identification of funds and other resources necessary to implement the plan, including interagency agreements on providing such funds and resources;

(4) methods to assure participation by the public in all phases of the planning process; and

[1] So in original. Probably should be "1990".

(5) such other methods as the Administrator determines necessary to carry out a continuous planning process.

(f)(1) The Administrator shall publish and make available to appropriate Federal, State, and local environmental and transportation agencies not later than one year after enactment of the Clean Air Act Amendments of 1990, and from time to time thereafter—

(A) information prepared, as appropriate, in consultation with the Secretary of Transportation, and after providing public notice and opportunity for comment, regarding the formulation and emission reduction potential of transportation control measures related to criteria pollutants and their precursors, including, but not limited to—

(i) programs for improved public transit;

(ii) restriction of certain roads or lanes to, or construction of such roads or lanes for use by, passenger buses or high occupancy vehicles;

(iii) employer-based transportation management plans, including incentives;

(iv) trip-reduction ordinances;

(v) traffic flow improvement programs that achieve emission reductions;

(vi) fringe and transportation corridor parking facilities serving multiple occupancy vehicle programs or transit service;

(vii) programs to limit or restrict vehicle use in downtown areas or other areas of emission concentration particularly during periods of peak use;

(viii) programs for the provision of all forms of high-occupancy, shared-ride services;

(ix) programs to limit portions of road surfaces or certain sections of the metropolitan area to the use of non-motorized vehicles or pedestrian use, both as to time and place;

(x) programs for secure bicycle storage facilities and other facilities, including bicycle lanes, for the convenience and protection of bicyclists, in both public and private areas;

(xi) programs to control extended idling of vehicles;

(xii) programs to reduce motor vehicle emissions, consistent with title II, which are caused by extreme cold start conditions;

(xiii) employer-sponsored programs to permit flexible work schedules;

(xiv) programs and ordinances to facilitate non-automobile travel, provision and utilization of mass transit, and to generally reduce the need for single-occupant vehicle travel, as part of transportation planning and development efforts of a locality, including programs and ordinances applicable to new shopping centers, special events, and other centers of vehicle activity;

(xv) programs for new construction and major reconstructions of paths, tracks or areas solely for the use by pedestrian or other non-motorized means of transportation

when economically feasible and in the public interest. For purposes of this clause, the Administrator shall also consult with the Secretary of the Interior; and

(xvi) program to encourage the voluntary removal from use and the marketplace of pre-1980 model year light duty vehicles and pre-1980 model light duty trucks.

(B) information on additional methods or strategies that will contribute to the reduction of mobile source related pollutants during periods in which any primary ambient air quality standard will be exceeded and during episodes for which an air pollution alert, warning, or emergency has been declared;

(C) information on other measures which may be employed to reduce the impact on public health or protect the health of sensitive or susceptible individuals or groups; and

(D) information on the extent to which any process, procedure, or method to reduce or control such air pollutant may cause an increase in the emissions or formation of any other pollutant.

(2) In publishing such information the Administrator shall also include an assessment of—

(A) the relative effectiveness of such processes, procedures, and methods;

(B) the potential effect of such processes, procedures, and methods on transportation system and the provision of transportation services; and

(C) the environmental, energy, and economic impact of such processes, procedures, and methods.

(3) The Secretary of Transportation and the Administrator shall submit to Congress by January 1, 1993, and every 3 years thereafter a report that—

(A) reviews and analyzes existing State and local air quality-related transportation programs, including specifically any analyses of whether adequate funding is available to complete transportation projects identified in State implementation plans in the time required by applicable State implementation plans and any Federal efforts to promote those programs;

(B) evaluates the extent to which the Department of Transportation's existing air quality-related transportation programs and such Department's proposed budget will achieve the goals of and compliance with this Act; and

(C) recommends what, if any, changes to such existing programs and proposed budget as well as any statutory authority relating to air quality-related transportation programs that would improve the achievement of the goals of and compliance with the Clean Air Act.

(4) In each report to Congress after the first report required under paragraph (3), the Secretary of Transportation shall include a description of the actions taken to implement the changes recommended in the preceding report.

(g) ASSESSMENT OF RISKS TO ECOSYSTEMS.—The Administrator may assess the risks to ecosystems from exposure to criteria air pollutants (as identified by the Administrator in the Administrator's sole discretion).

(h) RACT/BACT/LAER CLEARINGHOUSE.—The Administrator shall make information regarding emission control technology available to the States and to the general public through a central database. Such information shall include all control technology information received pursuant to State plan provisions requiring permits for sources, including operating permits for existing sources.

[42 U.S.C. 7408]

NATIONAL AMBIENT AIR QUALITY STANDARDS

SEC. 109. (a)(1) The Administrator—

(A) within 30 days after the date of enactment of the Clean Air Amendments of 1970, shall publish proposed regulations prescribing a national primary ambient air quality standard and a national secondary ambient air quality standard for each air pollutant for which air quality criteria have been issued prior to such date of enactment; and

(B) after a reasonable time for interested persons to submit written comments thereon (but no later than 90 days after the initial publication of such proposed standards) shall by regulation promulgate such proposed national primary and secondary ambient air quality standards with such modifications as he deems appropriate.

(2) With respect to any air pollutant for which air quality criteria are issued after the date of enactment of the Clean Air Amendments of 1970, the Administrator shall publish, simultaneously with the issuance of such criteria and information, proposed national primary and secondary ambient air quality standards for any such pollutant. The procedure provided for in paragraph (1)(B) of this subsection shall apply to the promulgation of such standards.

(b)(1) National primary ambient air quality standards, prescribed, under subsection (a) shall be ambient air quality standards the attainment and maintenance of which in the judgment of the Administrator, based on such criteria and allowing an adequate margin of safety, are requisite to protect the public health. Such primary standards may be revised in the same manner as promulgated.

(2) Any national secondary ambient air quality standard prescribed, under subsection (a) shall specify a level of air quality the attainment and maintenance of which in the judgment of the Administrator, based on such criteria, is requisite to protect the public welfare from any known or anticipated adverse effects associated with the presence of such air pollutant in the ambient air. Such secondary standards may be revised in the same manner as promulgated.

(c) The Administrator shall, not later than one year after the date of the enactment of the Clean Air Act Amendments of 1977, promulgate a national primary ambient air quality standard for NO_2 concentrations over a period of not more than 3 hours unless, based on the criteria issued under section 108(c), he finds that there is no significant evidence that such a standard for such a period is requisite to protect public health.

(d)(1) Not later than December 31, 1980, and at five-year intervals thereafter, the Administrator shall complete a thorough review of the criteria published under section 108 and the national ambient air quality standards promulgated under this section and shall make such revisions in such criteria and standards and promulgate such new standards as may be appropriate in accordance with section 108 and subsection (b) of this section. The Administrator may review and revise criteria or promulgate new standards earlier or more frequently than required under this paragraph.

(2)(A) The Administrator shall appoint an independent scientific review committee composed of seven members including at least one member of the National Academy of Sciences, one physician, and one person representing State air pollution control agencies.

(B) Not later than January 1, 1980, and at five-year intervals thereafter, the committee referred to in subparagraph (A) shall complete a review of the criteria published under section 108 and the national primary and secondary ambient air quality standards promulgated under this section and shall recommend to the Administrator any new national ambient air quality standards and revisions of existing criteria and standards as may be appropriate under section 108 and subsection (b) of this section.

(C) Such committee shall also (i) advise the Administrator of areas in which additional knowledge is required to appraise the adequacy and basis of existing, new, or revised national ambient air quality standards, (ii) describe the research efforts necessary to provide the required information, (iii) advise the Administrator on the relative contribution to air pollution concentrations of natural as well as anthropogenic activity, and (iv) advise the Administrator of any adverse public health, welfare, social, economic, or energy effects which may result from various strategies for attainment and maintenance of such national ambient air quality standards.

[42 U.S.C. 7409]

IMPLEMENTATION PLANS

SEC. 110. (a)(1) Each State shall, after reasonable notice and public hearings, adopt and submit to the Administrator, within 3 years (or such shorter period as the Administrator may prescribe) after the promulgation of a national primary ambient air quality standard (or any revision thereof) under section 109 for any air pollutant, a plan which provides for implementation, maintenance, and enforcement of such primary standard in each air quality control region (or portion thereof) within such State. In addition, such State shall adopt and submit to the Administrator (either as a part of a plan submitted under the preceding sentence or separately) within 3 years (or such shorter period as the Administrator may prescribe) after the promulgation of a national ambient air quality secondary standard (or revision thereof), a plan which provides for implementation, maintenance, and enforcement of such secondary standard in each air quality control region (or portion thereof) within such State. Unless a separate public hearing is provided, each State shall consider its plan implementing such secondary

standard at the hearing required by the first sentence of this paragraph.

(2) Each implementation plan submitted by a State under this Act shall be adopted by the State after reasonable notice and public hearing. Each such plan shall—

(A) include enforceable emission limitations and other control measures, means, or techniques (including economic incentives such as fees, marketable permits, and auctions of emissions rights), as well as schedules and timetables for compliance, as may be necessary or appropriate to meet the applicable requirements of this Act;

(B) provide for establishment and operation of appropriate devices, methods, systems, and procedures necessary to—

(i) monitor, compile, and analyze data on ambient air quality, and

(ii) upon request, make such data available to the Administrator;

(C) include a program to provide for the enforcement of the measures described in subparagraph (A), and regulation of the modification and construction of any stationary source within the areas covered by the plan as necessary to assure that national ambient air quality standards are achieved, including a permit program as required in parts C and D;

(D) contain adequate provisions—

(i) prohibiting, consistent with the provisions of this title, any source or other type of emissions activity within the State from emitting any air pollutant in amounts which will—

(I) contribute significantly to nonattainment in, or interfere with maintenance by, any other State with respect to any such national primary or secondary ambient air quality standard, or

(II) interfere with measures required to be included in the applicable implementation plan for any other State under part C to prevent significant deterioration of air quality or to protect visibility,

(ii) insuring compliance with the applicable requirements of sections 126 and 115 (relating to interstate and international pollution abatement);

(E) provide (i) necessary assurances that the State (or, except where the Administrator deems inappropriate, the general purpose local government or governments, or a regional agency designated by the State or general purpose local governments for such purpose) will have adequate personnel, funding, and authority under State (and, as appropriate, local) law to carry out such implementation plan (and is not prohibited by any provision of Federal or State law from carrying out such implementation plan or portion thereof), (ii) requirements that the State comply with the requirements respecting State boards under section 128, and (iii) necessary assurances that, where the State has relied on a local or regional government, agency, or instrumentality for the implementation of any plan provision, the State has responsibility for ensuring adequate implementation of such plan provision;

(F) require, as may be prescribed by the Administrator—

(i) the installation, maintenance, and replacement of equipment, and the implementation of other necessary steps, by owners or operators of stationary sources to monitor emissions from such sources,

(ii) periodic reports on the nature and amounts of emissions and emissions-related data from such sources, and

(iii) correlation of such reports by the State agency with any emission limitations or standards established pursuant to this Act, which reports shall be available at reasonable times for public inspection;

(G) provide for authority comparable to that in section 303 and adequate contingency plans to implement such authority;

(H) provide for revision of such plan—

(i) from time to time as may be necessary to take account of revisions of such national primary or secondary ambient air quality standard or the availability of improved or more expeditious methods of attaining such standard, and

(ii) except as provided in paragraph (3)(C), whenever the Administrator finds on the basis of information available to the Administrator that the plan is substantially inadequate to attain the national ambient air quality standard which it implements or to otherwise comply with any additional requirements established under this Act;

(I) in the case of a plan or plan revision for an area designated as a nonattainment area, meet the applicable requirements of part D (relating to nonattainment areas);

(J) meet the applicable requirements of section 121 (relating to consultation), section 127 (relating to public notification), and part C (relating to prevention of significant deterioration of air quality and visibility protection);

(K) provide for—

(i) the performance of such air quality modeling as the Administrator may prescribe for the purpose of predicting the effect on ambient air quality of any emissions of any air pollutant for which the Administrator has established a national ambient air quality standard, and

(ii) the submission, upon request, of data related to such air quality modeling to the Administrator;

(L) require the owner or operator of each major stationary source to pay to the permitting authority, as a condition of any permit required under this Act, a fee sufficient to cover—

(i) the reasonable costs of reviewing and acting upon any application for such a permit, and

(ii) if the owner or operator receives a permit for such source, the reasonable costs of implementing and enforcing the terms and conditions of any such permit (not including any court costs or other costs associated with any enforcement action),

until such fee requirement is superseded with respect to such sources by the Administrator's approval of a fee program under title V; and

(M) provide for consultation and participation by local political subdivisions affected by the plan.

(3) **[(A)]** [1]

(B) As soon as practicable, the Administrator shall, consistent with the purposes of this Act and the Energy Supply and Environmental Coordination Act of 1974, review each State's applicable implementation plans and report to the State on whether such plans can be revised in relation to fuel burning stationary sources (or persons supplying fuel to such sources) without interfering with the attainment and maintenance of any national ambient air quality standard within the period permitted in this section. If the Administrator determines that any such plan can be revised, he shall notify the State that a plan revision may be submitted by the State. Any plan revision which is submitted by the State shall, after public notice and opportunity for public hearing, be approved by the Administrator if the revision relates only to fuel burning stationary sources (or persons supplying fuel to such sources), and the plan as revised complies with paragraph (2) of this subsection. The Administrator shall approve or disapprove any revision no later than three months after its submission.

(C) Neither the State, in the case of a plan (or portion thereof) approved under this subsection, nor the Administrator, in the case of a plan (or portion thereof) promulgated under subsection (c), shall be required to revise an applicable implementation plan because one or more exemptions under section 118 (relating to Federal facilities), enforcement orders under section 113(d),[2] suspensions under section 110 (f) or (g) (relating to temporary energy or economic authority), orders under section 119 (relating to primary nonferrous smelters), or extensions of compliance in decrees entered under section 113(e) (relating to iron- and steel-producing operations) have been granted, if such plan would have met the requirements of this section if no such exemptions, orders, or extensions had been granted.

[(4)] [1]

(5)(A)(i) Any State may include in a State implementation plan, but the Administrator may not require as a condition of approval of such plan under this section, any indirect source review program. The Administrator may approve and enforce, as part of an applicable implementation plan, an indirect source review program which the State chooses to adopt and submit as part of its plan.

(ii) Except as provided in subparagraph (B), no plan promulgated by the Administrator shall include any indirect source review program for any air quality control region, or portion thereof.

(iii) Any State may revise an applicable implementation plan approved under section 110(a) to suspend or revoke any such program included in such plan, provided that such plan meets the requirements of this section.

(B) The Administrator shall have the authority to promulgate, implement and enforce regulations under section 110(c) respecting

[1] Subparagraph (A) was repealed by section 101(d)(1) of Public Law 101–549 (104 Stat. 2409).
[2] Section 113(d) was amended by section 701 of Public Law 101–549 (104 Stat. 2672) without conforming this reference.
[1] Paragraph (4) was repealed by section 101(d)(2) of Public Law 101–549 (104 Stat. 2409).

indirect source review programs which apply only to federally assisted highways, airports, and other major federally assisted indirect sources and federally owned or operated indirect sources.

(C) For purposes of this paragraph, the term "indirect source" means a facility, building, structure, installation, real property, road, or highway which attracts, or may attract, mobile sources of pollution. Such term includes parking lots, parking garages, and other facilities subject to any measure for management of parking supply (within the meaning of section 110(c)(2)(D)(ii)), including regulation of existing off-street parking but such term does not include new or existing on-street parking. Direct emissions sources or facilities at, within, or associated with, any indirect source shall not be deemed indirect sources for the purpose of this paragraph.

(D) For purposes of this paragraph the term "indirect source review program" means the facility-by-facility review of indirect sources of air pollution, including such measures as are necessary to assure, or assist in assuring, that a new or modified indirect source will not attract mobile sources of air pollution, the emissions from which would cause or contribute to air pollution concentrations—

(i) exceeding any national primary ambient air quality standard for a mobile source-related air pollutant after the primary standard attainment date, or

(ii) preventing maintenance of any such standard after such date.

(E) For purposes of this paragraph and paragraph (2)(B), the term "transportation control measure" does not include any measure which is an "indirect source review program".

(6) No State plan shall be treated as meeting the requirements of this section unless such plan provides that in the case of any source which uses a supplemental, or intermittent control system for purposes of meeting the requirements of an order under section 113(d)[1] or section 119 (relating to primary nonferrous smelter orders), the owner or operator of such source may not temporarily reduce the pay of any employee by reason of the use of such supplemental or intermittent or other dispersion dependent control system.

(b) The Administrator may, wherever he determines necessary, extend the period for submission of any plan or portion thereof which implements a national secondary ambient air-quality standard for a period not to exceed eighteen months from the date otherwise required for submission of such plan.

(c)(1) The Administrator shall promulgate a Federal implementation plan at any time within 2 years after the Administrator—

(A) finds that a State has failed to make a required submission or finds that the plan or plan revision submitted by the State does not satisfy the minimum criteria established under section 110(k)(1)(A), or

(B) disapproves a State implementation plan submission in whole or in part,

[1] See footnote 2 on page 34.

unless the State corrects the deficiency, and the Administrator approves the plan or plan revision, before the Administrator promulgates such Federal implementation plan.

(2) **[(A)]** [2]

(B) No parking surcharge regulation may be required by the Administrator under paragraph (1) of this subsection as a part of an applicable implementation plan. All parking surcharge regulations previously required by the Administrator shall be void upon the date of enactment of this subparagraph. This subparagraph shall not prevent the Administrator from approving parking surcharges if they are adopted and submitted by a State as part of an applicable implementation plan. The Administrator may not condition approval of any implementation plan submitted by a State on such plan's including a parking surcharge regulation.

[(C)] [3]

(D) For purposes of this paragraph—

(i) The term "parking surcharge regulation" means a regulation imposing or requiring the imposition of any tax, surcharge, fee, or other charge on parking spaces, or any other area used for the temporary storage of motor vehicles.

(ii) The term "management of parking supply" shall include any requirement providing that any new facility containing a given number of parking spaces shall receive a permit or other prior approval, issuance of which is to be conditioned on air quality considerations.

(iii) The term "preferential bus/carpool lane" shall include any requirement for the setting aside of one or more lanes of a street or highway on a permanent or temporary basis for the exclusive use of buses or carpools, or both.

(E) No standard, plan, or requirement, relating to management of parking supply or preferential bus/carpool lanes shall be promulgated after the date of enactment of this paragraph by the Administrator pursuant to this section, unless such promulgation has been subjected to at least one public hearing which has been held in the area affected and for which reasonable notice has been given in such area. If substantial changes are made following public hearings, one or more additional hearings shall be held in such area after such notice.

(3) Upon application of the chief executive officer of any general purpose unit of local government, if the Administrator determines that such unit has adequate authority under State or local law, the Administrator may delegate to such unit the authority to implement and enforce within the jurisdiction of such unit any part of a plan promulgated under this subsection. Nothing in this paragraph shall prevent the Administrator from implementing or enforcing any applicable provision of a plan promulgated under this subsection.

(5) [1](A) Any measure in an applicable implementation plan which requires a toll or other charge for the use of a bridge located entirely within one city shall be eliminated from such plan by the Administrator upon application by the Governor of the State, which

[2] Subparagraph (A) was repealed by section 101(d)(3) of Public Law 101–549 (104 Stat. 2409).
[3] Subparagraph (C) was repealed by section 101(d)(3) of Public Law 101–549, (104 Stat. 2409).
[1] Paragraph (4) was repealed by section 101(d)(3) of Public Law 101–549 (104 Stat. 2409).

application shall include a certification by the Governor that he will revise such plan in accordance with subparagraph (B).

(B) In the case of any applicable implementation plan with respect to which a measure has been eliminated under subparagraph (A), such plan shall, not later than one year after the date of the enactment of this subparagraph, be revised to include comprehensive measures to:

(i) establish, expand, or improve public transportation measures to meet basic transportation needs, as expeditiously as is practicable; and

(ii) implement transportation control measures necessary to attain and maintain national ambient air quality standards,

and such revised plan shall, for the purpose of implementing such comprehensive public transportation measures, include requirements to use (insofar as is necessary) Federal grants, State or local funds, or any combination of such grants and funds as may be consistent with the terms of the legislation providing such grants and funds. Such measures shall, as a substitute for the tolls or charges eliminated under subparagraph (A), provide for emissions reductions equivalent to the reductions which may reasonably be expected to be achieved through the use of the tolls or charges eliminated.

(C) Any revision of any implementation plan for purposes of meeting the requirements of subparagraph (B) shall be submitted in coordination with any plan revision required under part D.

[(d)] [1]
[(e)] [1]

(f)(1) Upon application by the owner or operator of a fuel burning stationary source, and after notice and opportunity for public hearing, the Governor of the State in which such source is located may petition the President to determine that a national or regional energy emergency exists of such severity that—

(A) a temporary suspension of any part of the applicable implementation plan [2] or any requirement under section 411 (concerning excess emissions penalties or offsets) of title IV of the Act may be necessary, and

(B) other means of responding to the energy emergency may be inadequate.

Such determination shall not be delegable by the President to any other person. If the President determines that a national or regional energy emergency of such severity exists, a temporary emergency suspension of any part of an applicable implementation plan [2] or any requirement under section 411 (concerning excess emissions penalties or offsets) of title IV of the Act adopted by the State may be issued by the Governor of any State covered by the President's determination under the condition specified in paragraph (2) and may take effect immediately.

(2) A temporary emergency suspension under this subsection shall be issued to a source only if the Governor of such State finds that—

(A) there exists in the vicinity of such source a temporary energy emergency involving high levels of unemployment or loss of necessary energy supplies for residential dwellings; and

(B) such unemployment or loss can be totally or partially alleviated by such emergency suspension.

Not more than one such suspension may be issued for any source on the basis of the same set of circumstances or on the basis of the same emergency.

(3) A temporary emergency suspension issued by a Governor under this subsection shall remain in effect for a maximum of four months or such lesser period as may be specified in a disapproval order of the Administrator, if any. The Administrator may disapprove such suspension if he determines that it does not meet the requirements of paragraph (2).

(4) This subsection shall not apply in the case of a plan provision or requirement promulgated by the Administrator under subsection (c) of this section, but in any such case the President may grant a temporary emergency suspension for a four month period of any such provision or requirement if he makes the determinations and findings specified in paragraphs (1) and (2).

(5) The Governor may include in any temporary emergency suspension issued under this subsection a provision delaying for a period identical to the period of such suspension any compliance

[1] Subsections (d) and (e) were repealed by section 101(d) of Public Law 101–549 (104 Stat. 2409). Subsection (d) is still referred to in section 404(b) of Public Law 95–620 (42 U.S.C. 8374(d)).

[2] Section 412 of Public Law 101–549 (104 Stat. 2634) amended section 110(f)(1) by inserting "or of any requirement under section 411 (concerning excess emissions penalties or offsets) of title IV of the Act" after "implmentation plan" without further specification. The words "implementation plan" appears in two places in section 110(f)(1).

schedule (or increment of progress) to which such source is subject under section 119, as in effect before the date of the enactment of this paragraph or section 113(d)[1] of this Act, upon a finding that such source is unable to comply with such schedule (or increment) solely because of the conditions on the basis of which a suspension was issued under this subsection.

(g)(1) In the case of any State which has adopted and submitted to the Administrator a proposed plan revision which the State determines—

(A) meets the requirements of this section, and

(B) is necessary (i) to prevent the closing for one year or more of any source of air pollution, and (ii) to prevent substantial increases in unemployment which would result from such closing, and

which the Administrator has not approved or disapproved under this section within 12 months of submission of the proposed plan revision, the Governor may issue a temporary emergency suspension of the part of the applicable implementation plan for such State which is proposed to be revised with respect to such source. The determination under subparagraph (B) may not be made with respect to a source which would close without regard whether or not the proposed plan revision is approved.

(2) A temporary emergency suspension issued by a Governor under this subsection shall remain in effect for a maximum of four months or such lesser period as may be specified in a disapproval order of the Administrator. The Administrator may disapprove such suspension if he determines that it does not meet the requirements of this subsection.

(3) The Governor may include in any temporary emergency suspension issued under this subsection a provision delaying for a period identical to the period of such suspension any compliance schedule (or increment of progress) to which such source is subject under section 119 as in effect before the date of the enactment of this paragraph, or under section 113(d)[1] upon a finding that such source is unable to comply with such schedule (or increment) solely because of the conditions on the basis of which a suspension was issued under this subsection.

(h)(1) Not later than 5 years after the date of enactment of the Clean Air Act Amendments of 1990, and every three years thereafter, the Administrator shall assemble and publish a comprehensive document for each State setting forth all requirements of the applicable implementation plan for such State and shall publish notice in the Federal Register of the availability of such documents.

(2) The Administrator may promulgate such regulations as may be reasonably necessary to carry out the purpose of this subsection.

(i) Except for a primary nonferrous smelter order under section 119, a suspension under section 110 (f) or (g) (relating to emergency suspensions), an exemption under section 118 (relating to certain Federal facilities), an order under section 113(d)[1] (relating to compliance orders), a plan promulgation under section 110(c), or a plan revision under section 110(a)(3), no order, suspension, plan

[1] See footnote 2 on page 34.

revision, or other action modifying any requirement of an applicable implementation plan may be taken with respect to any stationary source by the State or by the Administrator.

(j) As a condition for issuance of any permit required under this title, the owner or operator of each new or modified stationary source which is required to obtain such a permit must show to the satisfaction of the permitting authority that the technological system of continuous emission reduction which is to be used will enable such source to comply with the standards of performance which are to apply to such source and that the construction or modification and operation of such source will be in compliance with all other requirements of this Act.

(k) ENVIRONMENTAL PROTECTION AGENCY ACTION ON PLAN SUBMISSIONS.—

(1) COMPLETENESS OF PLAN SUBMISSIONS.—

(A) COMPLETENESS CRITERIA.—Within 9 months after the date of the enactment of the Clean Air Act Amendments of 1990, the Administrator shall promulgate minimum criteria that any plan submission must meet before the Administrator is required to act on such submission under this subsection. The criteria shall be limited to the information necessary to enable the Administrator to determine whether the plan submission complies with the provisions of this Act.

(B) COMPLETENESS FINDING.—Within 60 days of the Administrator's receipt of a plan or plan revision, but no later than 6 months after the date, if any, by which a State is required to submit the plan or revision, the Administrator shall determine whether the minimum criteria established pursuant to subparagraph (A) have been met. Any plan or plan revision that a State submits to the Administrator, and that has not been determined by the Administrator (by the date 6 months after receipt of the submission) to have failed to meet the minimum criteria established pursuant to subparagraph (A), shall on that date be deemed by operation of law to meet such minimum criteria.

(C) EFFECT OF FINDING OF INCOMPLETENESS.—Where the Administrator determines that a plan submission (or part thereof) does not meet the minimum criteria established pursuant to subparagraph (A), the State shall be treated as not having made the submission (or, in the Administrator's discretion, part thereof).

(2) DEADLINE FOR ACTION.—Within 12 months of a determination by the Administrator (or a determination deemed by operation of law) under paragraph (1) that a State has submitted a plan or plan revision (or, in the Administrator's discretion, part thereof) that meets the minimum criteria established pursuant to paragraph (1), if applicable (or, if those criteria are not applicable, within 12 months of submission of the plan or revision), the Administrator shall act on the submission in accordance with paragraph (3).

(3) FULL AND PARTIAL APPROVAL AND DISAPPROVAL.—In the case of any submittal on which the Administrator is required

to act under paragraph (2), the Administrator shall approve such submittal as a whole if it meets all of the applicable requirements of this Act. If a portion of the plan revision meets all the applicable requirements of this Act, the Administrator may approve the plan revision in part and disapprove the plan revision in part. The plan revision shall not be treated as meeting the requirements of this Act until the Administrator approves the entire plan revision as complying with the applicable requirements of this Act.

(4) CONDITIONAL APPROVAL.—The Administrator may approve a plan revision based on a commitment of the State to adopt specific enforceable measures by a date certain, but not later than 1 year after the date of approval of the plan revision. Any such conditional approval shall be treated as a disapproval if the State fails to comply with such commitment.

(5) CALLS FOR PLAN REVISIONS.—Whenever the Administrator finds that the applicable implementation plan for any area is substantially inadequate to attain or maintain the relevant national ambient air quality standard, to mitigate adequately the interstate pollutant transport described in section 176A or section 184, or to otherwise comply with any requirement of this Act, the Administrator shall require the State to revise the plan as necessary to correct such inadequacies. The Administrator shall notify the State of the inadequacies, and may establish reasonable deadlines (not to exceed 18 months after the date of such notice) for the submission of such plan revisions. Such findings and notice shall be public. Any finding under this paragraph shall, to the extent the Administrator deems appropriate, subject the State to the requirements of this Act to which the State was subject when it developed and submitted the plan for which such finding was made, except that the Administrator may adjust any dates applicable under such requirements as appropriate (except that the Administrator may not adjust any attainment date prescribed under part D, unless such date has elapsed).

(6) CORRECTIONS.—Whenever the Administrator determines that the Administrator's action approving, disapproving, or promulgating any plan or plan revision (or part thereof), area designation, redesignation, classification, or reclassification was in error, the Administrator may in the same manner as the approval, disapproval, or promulgation revise such action as appropriate without requiring any further submission from the State. Such determination and the basis thereof shall be provided to the State and public.

(l) PLAN REVISIONS.—Each revision to an implementation plan submitted by a State under this Act shall be adopted by such State after reasonable notice and public hearing. The Administrator shall not approve a revision of a plan if the revision would interfere with any applicable requirement concerning attainment and reasonable further progress (as defined in section 171), or any other applicable requirement of this Act.

(m) SANCTIONS.—The Administrator may apply any of the sanctions listed in section 179(b) at any time (or at any time after) the Administrator makes a finding, disapproval, or determination

under paragraphs (1) through (4), respectively, of section 179(a) in relation to any plan or plan item (as that term is defined by the Administrator) required under this Act, with respect to any portion of the State the Administrator determines reasonable and appropriate, for the purpose of ensuring that the requirements of this Act relating to such plan or plan item are met. The Administrator shall, by rule, establish criteria for exercising his authority under the previous sentence with respect to any deficiency referred to in section 179(a) to ensure that, during the 24-month period following the finding, disapproval, or determination referred to in section 179(a), such sanctions are not applied on a statewide basis where one or more political subdivisions covered by the applicable implementation plan are principally responsible for such deficiency.

(n) SAVINGS CLAUSES.—

(1) EXISTING PLAN PROVISIONS.—Any provision of any applicable implementation plan that was approved or promulgated by the Administrator pursuant to this section as in effect before the date of the enactment of the Clean Air Act Amendments of 1990 shall remain in effect as part of such applicable implementation plan, except to the extent that a revision to such provision is approved or promulgated by the Administrator pursuant to this Act.

(2) ATTAINMENT DATES.—For any area not designated nonattainment, any plan or plan revision submitted or required to be submitted by a State—

(A) in response to the promulgation or revision of a national primary ambient air quality standard in effect on the date of the enactment of the Clean Air Act Amendments of 1990, or

(B) in response to a finding of substantial inadequacy under subsection (a)(2) (as in effect immediately before the date of the enactment of the Clean Air Act Amendments of 1990),

shall provide for attainment of the national primary ambient air quality standards within 3 years of the date of the enactment of the Clean Air Act Amendments of 1990 or within 5 years of issuance of such finding of substantial inadequacy, whichever is later.

(3) RETENTION OF CONSTRUCTION MORATORIUM IN CERTAIN AREAS.—In the case of an area to which, immediately before the date of the enactment of the Clean Air Act Amendments of 1990, the prohibition on construction or modification of major stationary sources prescribed in subsection (a)(2)(I) (as in effect immediately before the date of the enactment of the Clean Air Act Amendments of 1990) applied by virtue of a finding of the Administrator that the State containing such area had not submitted an implementation plan meeting the requirements of section 172(b)(6) (relating to establishment of a permit program) (as in effect immediately before the date of enactment of the Clean Air Act Amendments of 1990) or 172(a)(1) (to the extent such requirements relate to provision for attainment of the primary national ambient air quality standard for sulfur oxides by December 31, 1982) as in effect immediately before the date of the enactment of the Clean Air

Act Amendments of 1990, no major stationary source of the relevant air pollutant or pollutants shall be constructed or modified in such area until the Administrator finds that the plan for such area meets the applicable requirements of section 172(c)(5) (relating to permit programs) or subpart 5 of part D (relating to attainment of the primary national ambient air quality standard for sulfur dioxide), respectively.

(o) INDIAN TRIBES.—If an Indian tribe submits an implementation plan to the Administrator pursuant to section 301(d), the plan shall be reviewed in accordance with the provisions for review set forth in this section for State plans, except as otherwise provided by regulation promulgated pursuant to section 301(d)(2). When such plan becomes effective in accordance with the regulations promulgated under section 301(d), the plan shall become applicable to all areas (except as expressly provided otherwise in the plan) located within the exterior boundaries of the reservation, notwithstanding the issuance of any patent and including rights-of-way running through the reservation.

(p) REPORTS.—Any State shall submit, according to such schedule as the Administrator may prescribe, such reports as the Administrator may require relating to emission reductions, vehicle miles traveled, congestion levels, and any other information the Administrator may deem necessary to assess the development effectiveness, need for revision, or implementation of any plan or plan revision required under this Act.

[42 U.S.C. 7410]

STANDARDS OF PERFORMANCE FOR NEW STATIONARY SOURCES

SEC. 111. (a) For purposes of this section:

(1) The term “standard of performance” means a standard for emissions of air pollutants which reflects the degree of emission limitation achievable through the application of the best system of emission reduction which (taking into account the cost of achieving such reduction and any nonair quality health and environmental impact and energy requirements) the Administrator determines has been adequately demonstrated.

For the purpose of subparagraphs (A) (i) and (ii) and (B), a standard of performance shall reflect the degree of emission limitation and the percentage reduction achievable through application of the best technological system of continuous emission reduction which (taking into consideration the cost of achieving such emission reduction, any nonair quality health and environmental impact and energy requirements) the Administrator determines has been adequately demonstrated. For the purpose of subparagraph[1] (1)(A)(ii), any cleaning of the fuel or reduction in the pollution characteristics of the fuel after extraction and prior to combustion may be credited, as determined under regulations promulgated by the Administrator, to a source which burns such fuel.

[1] So in original. Probably should be “paragraph”.

CERTIFICATE OF SERVICE

I hereby certify that on this 30th day of April, 2012, I served the counsel of record listed below the foregoing **Petitioners' and Petitioner-Intervenor's Opening Brief** by dispatching a hard copy to a third party commercial service for copying and delivery. Counsel of record are:

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Addendum B

UNITED STATES COURT OF APPEALS
FOR THE DISTRICT OF COLUMBIA CICUIT

COMMUNITIES FOR A BETTER ENVIRONMENT and WILDEARTH GUARDIANS, Petitioners, v. UNITED STATES ENVIRONMENTAL PROTECTION AGENCY, Respondent.	Case No. 11-1423

DECLARATION OF ALBERT DONNAY
IN SUPPORT OF PETITIONERS' OPENING BRIEF

Declaration of Albert Donnay

I, Albert Donnay, declare as follows:

1. The facts set forth in this declaration are based on my personal knowledge, experience, training, review of the pertinent literature, and reanalysis of published data. If called as a witness, I could and would testify to these facts. As to those matters that reflect an opinion, they reflect my expert opinion and judgment on the matter.

2. I am an independent consulting toxicologist and environmental health engineer.

3. I received my Bachelor of Arts in Mathematics from McGill University in 1980. I then earned a Masters of Health Sciences in Environmental Health Engineering from Johns Hopkins School of Public Health in 1983.

4. I am currently a Doctoral candidate in Toxicology at the University of Maryland at Baltimore and expect to complete the program in 2012.

5. I have 14 years of experience researching, writing and speaking about CO-related issues.

6. My areas of expertise include CO-related medical disorders, sources of CO exposure (both exogenous and endogenous, from outside and within the human body), CO detectors, CO policies and regulations, and CO-related training for medical and public health professionals.

7. I designed the first low-level home CO detector sold in USA (for AIM SafeAir Products in 1999); developed the first protocol for measuring CO emissions from appliances, vehicles and human breath using portable CO detectors; developed the first protocol for screening, testing and treating chronic CO poisoning; and co-authored and co-performed a one-hour CME-accredited "Historic Grand Rounds" about CO at the first International Symposium on Heme Oxygenase and Carbon Monoxide in 2000 entitled: "The Illness and Death of Edgar Allan Poe" (subsequently performed at the National Library of Medicine).

8. I have contributed to peer-reviews of CO-related documents for local, state and federal government agencies (including EPA), and advocated pro bono for more protective standards for CO detectors and CO-generating appliances from governments and independent standard-setting organizations.

9. In 2001, I petitioned US NHTSA to require the installation of CO detectors in motor vehicles, and in 2011, I submitted public comments to EPA in support of my professional opinion that the current CO National Ambient Air Quality Standards (NAAQS) limits are inadequate to protect public health. I did so in my own name, in a petition signed by over 100 others, and in a statement co-authored by Physicians for Social Responsibility.

Introduction

10. It is my expert opinion that the NAAQS adopted by the US Environmental Protection Agency (EPA) on August 31, 2011, is inadequate to “protect public health,” including the

health of sensitive populations, with an adequate "margin of safety" as the Clean Air Act requires.

11. When first adopted in 1971, EPA's CO NAAQS limits of 9 parts per million (ppm) average over 8 hours and 35ppm over 1 hour were much lower than CO levels in most large US cities, which then averaged over 35ppm.[1] But—unrelated to EPA's unchanged CO standard—average CO levels are now much lower than the CO NAAQS, with the national annual (second) highest 8-hour average falling from 6.2ppm in 1990 to 1.8ppm in 2009.[2]

12. Perversely, because EPA never lowered the CO NAAQS to keep pace with this declining trend, the standard now offers manufacturers of CO sources such as vehicles and power plants a large margin of safety from regulation within which they can increase CO emissions.

13. Under EPA's CO NAAQS, average outdoor CO levels in most American cities could quadruple and still not exceed EPA's 8-hour limit, while the average 1-hour exposure could increase 9-fold.

14. In contrast, the margin of safety protecting people from the adverse health effects of CO has not changed in 30 years, despite the publication of over 18,000 peer-reviewed studies on CO during this time. In this review commenters, including myself, presented EPA with 393 (Attachment A) studies on various health effects of CO which EPA ignored in it's review.

15. The CO NAAQS rule published by EPA in 2011 is based primarily on a single controlled exposure study of just 63 men with coronary artery disease (CAD) and stable exertional angina (SEA) (the Allred study, 1989).[3]

16. EPA's confidence in the Allred study is not warranted given numerous problems with its design, methods and publication. But even if the study is valid, it does not actually support the current CO NAAQS because approximately one-third of the subjects experienced a worsening of their angina despite COHb levels below EPA's 2% "margin of safety."

17. An even larger percentage of the subjects in this key study benefited from their CO exposures. Specifically, they were able to exercise longer before the onset of angina and/or a more objective indicator of myocardial ischemia (MI) called ST segment depression as measured by EKG. This was an unexpected finding at the time. The Allred study hypothesized that exposure to CO would only worsen these biomarkers of MI in people with CAD/SEA. But it is now well-recognized in more recent CO literature that "CO has anti-inflammatory

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[1] EPA. National primary and secondary air quality standard. April 30, 1971. Federal Register 36(84):8186-8201

[2] EPA data on CO emissions trends accessed online 3/21/12 at http://cfpub.epa.gov/eroe/index.cfm?fuseaction=detail.viewInd&lv=list.listbyalpha&r=231329&subtop=341

[3] Allred EN, Bleecker ER, Chaitman BR, Dahms TE, Gottlieb SO, Hackney JD, Hayes D, Pagano M, Selvester RH, Walden SM, et al. Acute effects of carbon monoxide exposure on individuals with coronary artery disease. Res Rep Health Eff Inst. 1989 Nov;(25):1-79.
Published simultaneously as Allred EN, Bleecker ER, Chaitman BR, Dahms TE, Gottlieb SO, Hackney JD, Pagano M, Selvester RH, Walden SM, Warren J. Short-term effects of carbon monoxide exposure on the exercise performance of subjects with coronary artery disease. N Engl J Med. 1989 Nov 23;321(21):1426-32. Erratum in: N Engl J Med 1990 Apr 5;322(14):1019.
Published two years later as: Allred EN, Bleecker ER, Chaitman BR, Dahms TE, Gottlieb SO, Hackney JD, Pagano M, Selvester RH, Walden SM, Warren J. Effects of carbon monoxide on myocardial ischemia. Environ Health Perspect. 1991 Feb;91:89-132

properties and that administration of CO provides protection against atherosclerosis and ischemic heart disease."[4]

18. The highly variable and inconsistent response to CO seen among the 63 men with CAD/SEA in the Allred study means that the results cannot be meaningfully extrapolated to any other population. The integrity of EPA's CO NAAQS also is undermined by many deviations from EPA's normal NAAQS review procedures as well as by many deficiencies in and omissions from the scientific literature that EPA considered and relied upon in this rulemaking.

Basis of CO NAAQS

19. The fact that outdoor CO exposures in the US are commonly far below the NAAQS does not mean EPA need not be concerned about the health risks of small increases in CO exposure within the current ambient range. In fact, it is precisely those CO-related health risks, which remain evident at exposures below the NAAQS which should be of most concern.

20. Unfortunately, unlike with particulates, EPA did not base its CO assessment on data from environmental epidemiology (EE) studies that can quantify the increased risks for various adverse events such as hospitalizations and deaths from heart attacks associated with small increases in ambient exposure that may persist for hours or days before dissipating.

21. EPA based it instead on a quantified risk and exposure assessment that was informed by modeling CO exposure data from just two US cities, Los Angeles and Denver. Given the great variability in peak CO exposures nationwide—as reflected in EPA's list of cities and counties both large and small that still have higher than average CO levels--these are insufficiently representative samples on which to model the entire US population.

22. EPA claims its risk modeling accurately identifies the maximum average CO exposure for adults and children (for either 1 or 8 hours) that will not raise CO in their blood to levels associated with the significant adverse effects seen in controlled exposure studies. The marker of CO "uptake" favored by EPA and commonly used in controlled exposure studies is the percentage of hemoglobin in venous (v) blood that is bound to carbon monoxide, called (v) carboxyhemoglobin or %(v)COHb.

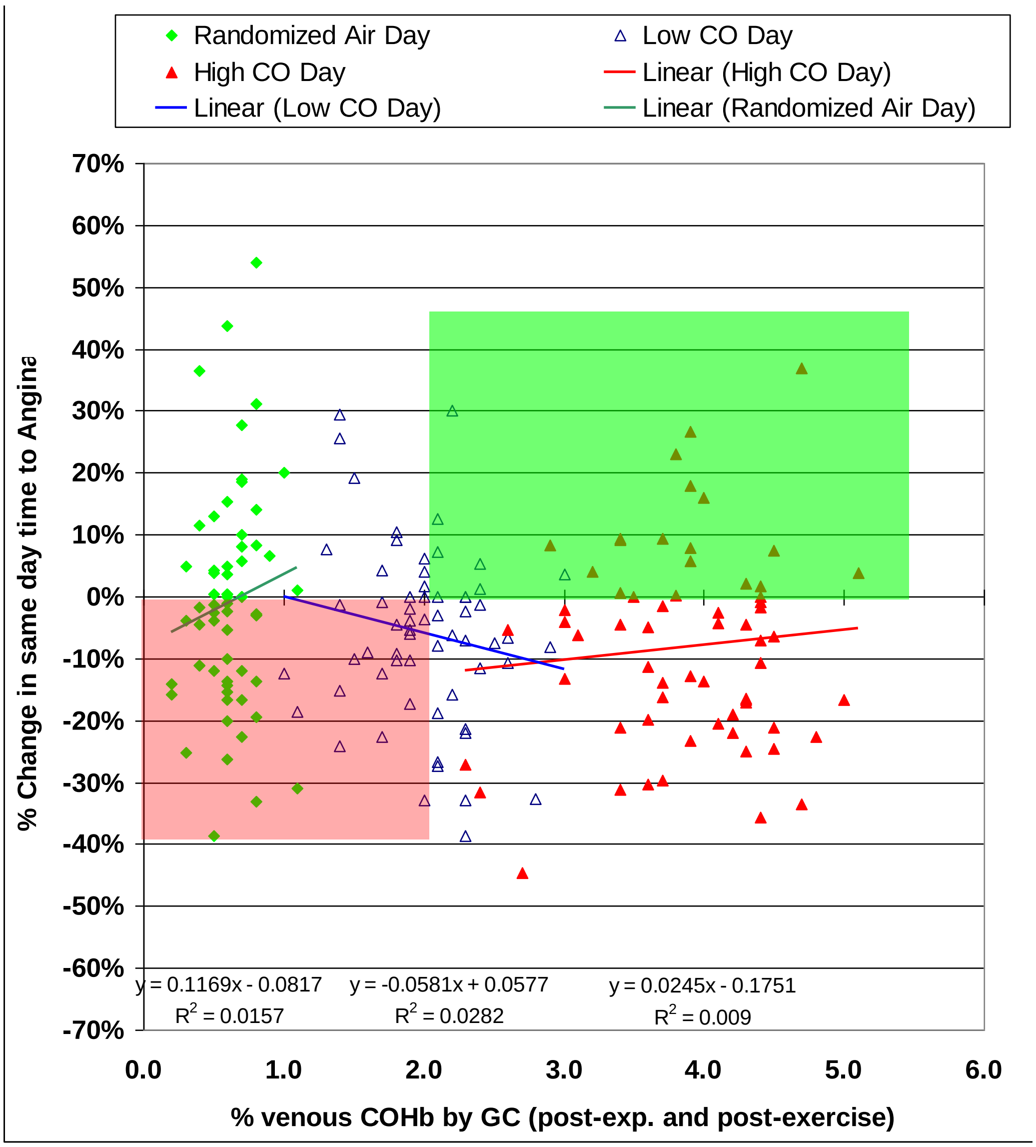
23. Venous blood is preferred in CO studies because it is easier and less painful to sample. Critically, venous blood does not oxygenate tissue, but primarily brings gases that have diffused out of tissues back to the lungs for exhalation. As such, %(v)COHb is actually a measure of CO elimination rather than uptake. Neither venous CO or oxygen levels have much effect on heart function, in contrast to arterial levels, on which heart function critically depends via the coronary arteries.

24. Citing the Allred study, EPA specifies that CO exposure limits should be set to keep %(v)COHb levels under the 2.0% mean level at which adverse effects were seen on the low CO exposure day. But Allred et al. actually found that adverse effects of concern after exposure occurred across a wide range of %(v)COHb on that day, from 1.0% to 3.0% (red area of Figure

[4] Ozono R. New biotechnological methods to reduce oxidative stress in the cardiovascular system: focusing on the Bach1/heme oxygenase-1 pathway. Curr Pharm Biotechnol. 2006 Apr;7(2):87-93.

1 shows results for angina). In contrast, many others were able to exercise longer until angina after low and/or high dose CO exposures, despite ending up with %(v)COHb levels above EPA's 2% threshold. (green area of Figure 1).

Figure 1. Percent change in time to angina after breathing air, low CO and high CO
Source = Allred data plotted by Donnay and color-coded by type of exposure
Note 1: Range of %(v)COHb by on air day=0.2-1.1, low CO day=1.0-3.0, high CO day=2.3, 5.1
Note 2: Area in pink shows subjects not protected by CO NAAQS whose time to angina during exercise was shorter after exposure to air or CO despite %(v)COHb below 2% margin of safety.
Note 3: Area in green shows subjects whose time to angina was same or longer after CO exposure compared to before despite %(v)COHb above 2% margin of safety.1



25. EPA's proposed and final CO NAAQS rules never disclose the full range of %(v)COHb at which adverse effects were seen, but instead always report the lowest observed level of the Allred study only as 2%. Given that EPA's primary adverse effect of greatest concern was

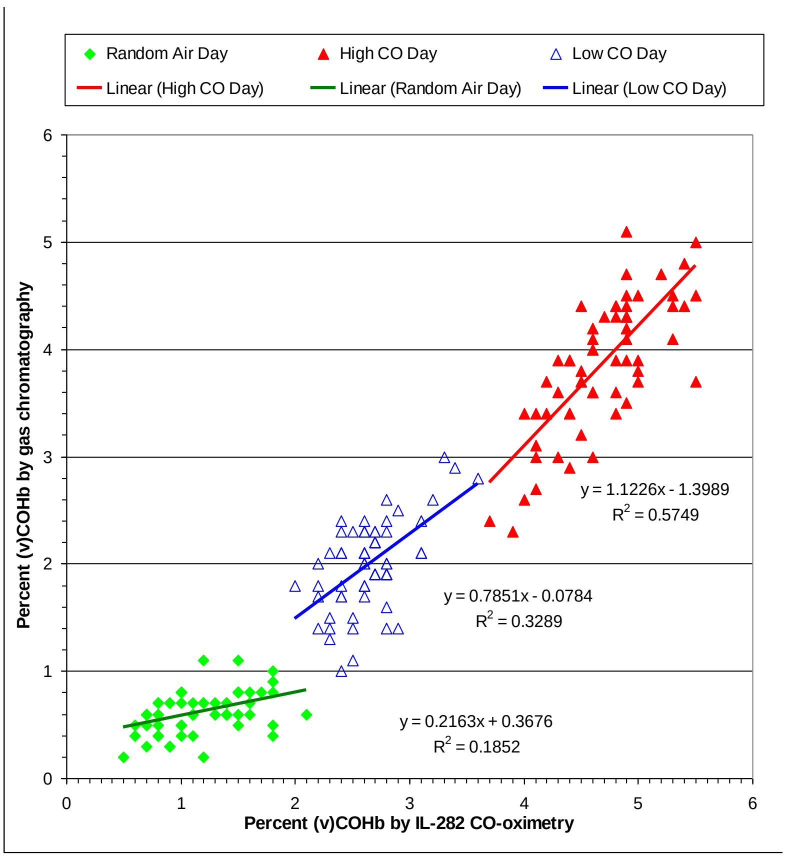
actually observed at just half this level, the CO NAAQS is set too high to protect them.

26. EPA's error is clear in a footnote in the final rule in which it discusses two of three COHb measurement methods used in the Allred study, namely gas chromatography (GC) and CO-oximetry (COOx).

27. EPA correctly noted that for GC, "… the COHb blood level for each subject during the exercise tests as determined was intermediate between the post-exposure and subsequent post-exercise measurements."[5] Its error was in then suggesting that the range of these measurements on the low and high CO exposure days fell within the difference of their means: "(e.g., mean 2.4–2.0%. and 4.7–3.9%)." This is mathematically impossible.

28. EPA then repeats this error in the next sentence, while also misleadingly reversing the order of the pre and post-exercise COHb means being reported. It says the "corresponding ranges of COOx measurements for the two exposures were 2.7–3.2% and 4.7–5.6%," but as with the GC measurements of COHb, EPA never disclosed these actual ranges (Figure 2).

Figure 2. Precision of COHb measurement methods
Source: Allred data plotted by Donnay and color-coded by type of exposure
Note 1: all measurements are of venous samples drawn post-exposure and post-exercise
Note 2: each measure is the average of analyses run in triplicate for each method.



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[5] EPA. Review of National Ambient Air Quality Standards for Carbon Monoxide. August 31, 2011. Federal Register 76(169): 54306. footnote 15

29. EPA never acknowledged the poor agreement between the two methods used to measure COHb (gas chromatography - GC and co-oximetry - COOx), or that the slope of this correlation varied widely with the range of COHb being measured. At any specific level of %(v)COHb as measured by GC, the same measurements by COOx were widely scattered. The reverse is also true. The scatter is wide that, EPA should have included an uncertainty factor in its CO risk assessment to account for it.

30. The five other smaller controlled CO exposures that EPA says are consistent with Allred and also supportive of the CO NAAQS all used this less accurate COOx method. Regardless of these COHb measurement errors, however, the greater error was EPA's misrepresentation of all their results by their means instead of their ranges.

31. It also is completely unjustified for EPA to cite the average COHb levels reported in these studies to one decimal place as if accurate and representative when the actual results were so widely distributed. The target levels of %(v)COHb that Allred study sought to achieve in these subjects were 2% and 4% %(v)COHb, but as shown in Figure 2 above, the actual ranges of COHb achieved were 1.0 to 3.0 on the 2% target day and 2.3 to 5.1% on the 4% day (all per GC).

32. Note that any detectable levels of arterial and venous COHb are never solely the result of some external CO exposure. All humans continuously make and metabolize CO.

33. Most comes from the normal breakdown of heme proteins such hemoglobin but also myoglobin, neuroglobin and cytochromes found throughout our bodies. This is why all healthy humans have CO detectable in both their blood (as COHb, usually under 1%) and in their exhaled breath in parts per million (ppm).

34. Once in tissues, inhaled CO may be metabolized into carbon dioxide if sufficient oxygen is available or it may be bind to other heme proteins such as cytochromes in mitochondria, myoglobin in muscle, and neuroglobin in nerves. Literally hundreds of biochemical pathways have been identified in humans and other mammals in which CO plays a functional or catalytic role.[6] In healthy non-smokers, exhaled CO is normally less than 3ppm but in various diseases it ranges from 5 to 15ppm.

35. As the level of CO bound to these proteins increases, it interferes with their ability to also bind oxygen, which is thought to be the primary mechanism of CO toxicity. The overall effect of increasing CO exposure is to reduce the amount of oxygen available for muscular work and other types of metabolism.

36. In short-term, very high CO exposures (CO poisoning) arterial COHb ((a)COHB) rises much more quickly than does venous COHb ((v)COHb). The difference ((a-v)COHb) between them may grow to several percent before equilibrium is reached, at which point a difference of 0.5% is typical.

[6] Ryter SW, Choi AM. Heme oxygenase-1/carbon monoxide: from metabolism to molecular therapy. Am J Respir Cell Mol Biol. 2009 Sep;41(3):251-60.

37. As soon as the exposure ends, %(a)COHb starts to fall rapidly but %(v)COHb continues to rise as CO leaves the body until it is slightly higher than arterial.

38. This new equilibrium is notable, however, because the normal a-v COHb difference is reversed such that COHb is higher on the venous side. This state continues while the absorbed CO is excreted.

39. This excretion takes much longer than did the absorption during poisoning, due to the slow rate at which absorbed CO diffuses from tissues back into venous blood. It can be sped up by any exercise which increases the breathing rate. It also is immediately reversed by any new CO exposures and so may never stabilize in individuals who experience frequent significant CO exposures.

40. The higher the CO exposure, the more quickly equilibrium is reached. (This is why smokers are not immediately sickened as non-smokers are by absorbing hundreds to thousands of ppm of CO with each inhalation.)

41. At exposure levels below the current CO NAAQS, however, experimental evidence cited by EPA shows it takes at least 24 hours for the %(v)COHb to peak.[7]

42. The longest form of EPA's CO NAAQS, however, is only an 8-hour maximum average. EPA adopted the 8-hour limit on the assumption that "approximately 4-12 hours are required to achieve an equilibrium level of COHb."[8] Based on a classic controlled exposure study done later in the 1970s, however—which EPA cites in the 2010 ISA—it takes at least 24 hours for %(v)COHb to stop rising when CO levels are under 25ppm. Only at exposures above 1000ppm is equilibrium reached within 8 hours or less.[9]

43. Given the relative seasonal stability of ambient CO levels as reported by EPA (highest in winter and lowest in summer), most people's exposure to ambient CO is not 8 hours per day but 24 hours per day. In fact, data from EE studies show that small increases in average CO exposure of up to a few ppm may persist for a week or more in urban areas.

44. So regardless of the accuracy of EPA's CO risk modeling efforts, the CO NAAQS is at best and by design only able to protect people from reaching a particular %(v)COHb level within 8 hours of exposure.

45. The CO NAAQS does not protect people from the higher %(v)COHb level that inevitably arise whenever ambient CO levels stay elevated for more than 8 hours.

46. (v)COHb does not increase linearly over time, but rises slowly at first and then more steeply before finally gradually leveling off again as a new higher level of equilibrium is reached. The (v)COHb levels that EPA's modeling predicts will result from any 8-hour CO

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[7] Peterson JE, Stewart RD. Predicting the carboxyhemoglobin levels resulting from carbon monoxide exposures. J Appl Physiol. 1975 Oct;39(4):633-8

[8] EPA. Review of National Ambient Air Quality Standards for Carbon Monoxide. Federal Register. August 18, 1980. 45(161):55077

[9] Peterson JE, Stewart RD. Predicting the carboxyhemoglobin levels resulting from carbon monoxide exposures. J Appl Physiol. 1975 Oct;39(4):633-8

exposure are thus not even one-third the level that experimental data show would eventually be reached if the same exposure level were inhaled for 24 hours.[10]

47. As discussed in more detail below, dose is defined in traditional toxicology as the product of the exposure concentration and exposure time. In case of the CO NAAQS therefore, which allows exposures to maximum average CO doses of 35ppm for 1hour and 9ppm for 8 hours, the result is doses of 35 and 72ppm* hours, respectively. Note that the lower standard actually allows inhalation of more than twice the total dose.

48. When EPA first proposed revising the CO NAAQS in 1980, it focused only on lowering the 1-hour standard (from 35 to 25ppm average), under the mistaken assumption that shorter more acute CO exposures posed greater risks than longer and lower exposures.[11] This is not always true, as has been noted in the clinical literature on CO poisoning for decades.

49. The reason—exemplified by EPA's CO NAAQS—is that low CO exposure levels may result in much larger total inhaled doses over time compared to brief but high level exposures that usually do not last as long.

50. The longest CO exposure period in the controlled exposure studies upon which EPA places most emphasis was just two hours.[12] Because this is far too short for %(v)COHb to reach equilibrium at any dose, such studies should not be relied upon to predict how high %(v)COHb may rise if exposures continue beyond 8 hours, which the CO NAAQS allows.

51. Because EPA's CO NAAQS allows average CO levels to remain elevated across multiple 8 hour periods, it is effectively a 24-hour standard as well, with a 9ppm average limit overall as well as within each 8-hour period.

52. EPA's current standard thus allows a 24-hour exposure of 216ppm* hours (ppmh). Such a high dose will have a greater adverse effect on anyone than exposure to 35ppm average for 1 hour (=35ppmh) or 9ppm for 8 hours (=72ppmh).

53. Even if, as is much more likely under current ambient conditions, Americans were exposed to only 4ppm average every 8 hours, they would still over the course of 24 hours reach 96ppmh and so exceed the total dose allowed by EPA's current 8-hour standard.

54. Throughout EPA's CO NAAQS review process, from the Integrated Science Assessment (ISA) through the Risk and Exposure Assessment (REA), Policy Assessment (REA), Policy Assessment (PA) and proposed rule, neither the agency or EPA's Clean Air Scientific Advisory Committee CO Advisory Panel (the CO CASAC) ever discussed the implications of average ambient CO exposures above zero that last longer than just 8 hours. But such data are available from the time series analyses commonly done in EE studies, and EPA should have acknowledged the implications of their results, which are discussed below.

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[10] Ibid.

[11] EPA. Review of National Ambient Air Quality Standards for Carbon Monoxide. August 18, 1980. Federal Register 45(161):55066-54343

[12] Kleinman MT, Leaf DA, Kelly E, Caiozzo V, Osann K, O'Niell T. Urban angina in the mountains: effects of carbon monoxide and mild hypoxemia on subjects with chronic stable angina. Arch Environ Health. 1998;53(6):388-97.

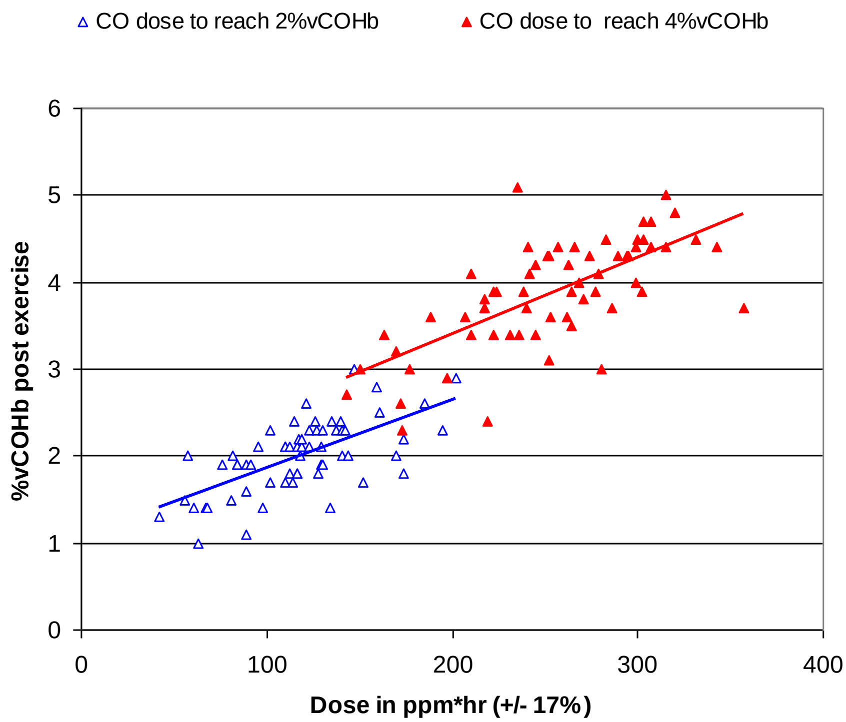
Allred data on Inhaled CO Dose vs Excreted %(v)COHb

55. EPA defends basing the CO NAAQS on a COHb threshold because "much of the broader health effects evidence for CO, and particularly that related to cardiovascular effects, demonstrates and focuses on an internal biomarker of CO exposure (COHb)."

56. It correctly notes that "CO epidemiological studies use a different exposure/dose metric" (equal to the product of the concentration of CO in air and the duration of exposure), "from that which is the focus of the broader health evidence base," but it errs in concluding that "additional information that might be used to bridge this gap is lacking."[13]

57. Fortunately, all of the controlled CO exposure studies that EPA cites in support of the CO NAAQS, including Allred, published raw data that included both the level and at least an approximate duration, if not the exact time of each subject's CO exposure. From these data the standard dose can be calculated (=concentration x time) and compared with the levels of %(v)COHb that resulted (Figure 3).

Figure 3. Relationship between inhaled CO dose and resulting venous COHb
Source: Allred data plotted by Donnay and color-coded by type of exposure
Note 1: Air days not shown because all doses less than 5ppmh



58. The results of this correlation are extremely poor, with wide ranges of scatter in both directions and a significant shift in the linear regression correlation between these measures on the low CO days (in blue above) compared to the high CO days. Assuming the study used the

[13] EPA. Review of National Ambient Air Quality Standards for Carbon Monoxide. August 31, 2011. Federal Register 76(169): 54306. [This and all other EPA documents related to this rulemaking are available online at http://www.epa.gov/ttn/naaqs/standards/co/s_co_index.html.]

same instruments on both low and high CO days, the slopes and y-axis intercepts of these regression lines should have been statistically identical.

59. Neither Allred or EPA gives any explanation of the discrepancy, but it appears to be related to the unnaturally tight clustering of the low dose (blue) data points around the 2% line. If these data were more loosely scattered as are the data from the high CO day, their regression lines would have been much closer together.

60. Another serious issue evident from this figure is the fact that subjects' responses overlapped, as did the resulting levels of %(v)COHb.

61. The Allred study used different doses for all subjects that were titrated to their individual rates of %(v)COHb formation. The goal was for everyone to reach the same target levels of %(v)COHb at the end of their exposure and exercise, namely 2% on the low CO day and 4% on the high. Given the overlapping responses noted just above, there were not two distinct doses, but rather a range of doses.

62. The range of exposures (on the x-axis) that resulted in any particular %(v)COHb level (on the y-axis) was wide, from two to three-fold. The results clearly should have been analyzed the exposure data (dose or COHb) in the form of a continuous variable rather than as the discrete group means.

63. Given that EPA can only regulate CO emissions and has no control over the myriad variables that influence %(v)COHb, the CO NAAQS should be based instead on correlations between adverse effects and exposure rather than with %(v)COHb.

64. There is simply too much human variation in response to any given CO dose to establish scientifically meaningful CO exposure limits based on %(v)COHb alone.

65. It is much easier, less expensive, faster and more accurate to estimate absorbed CO based on differences in the CO concentration of inhaled and exhaled air. (This is the basis of a common pulmonary function test called the Diffusing Capacity of the Lung for CO or DLCO which has been in widespread use for over 50 years.)

66. Both EPA's 1-hour and 8-hour CO NAAQS can easily be converted into maximum inhaled doses of 35ppm* hours (ppmh) and 72ppmh, respectively.

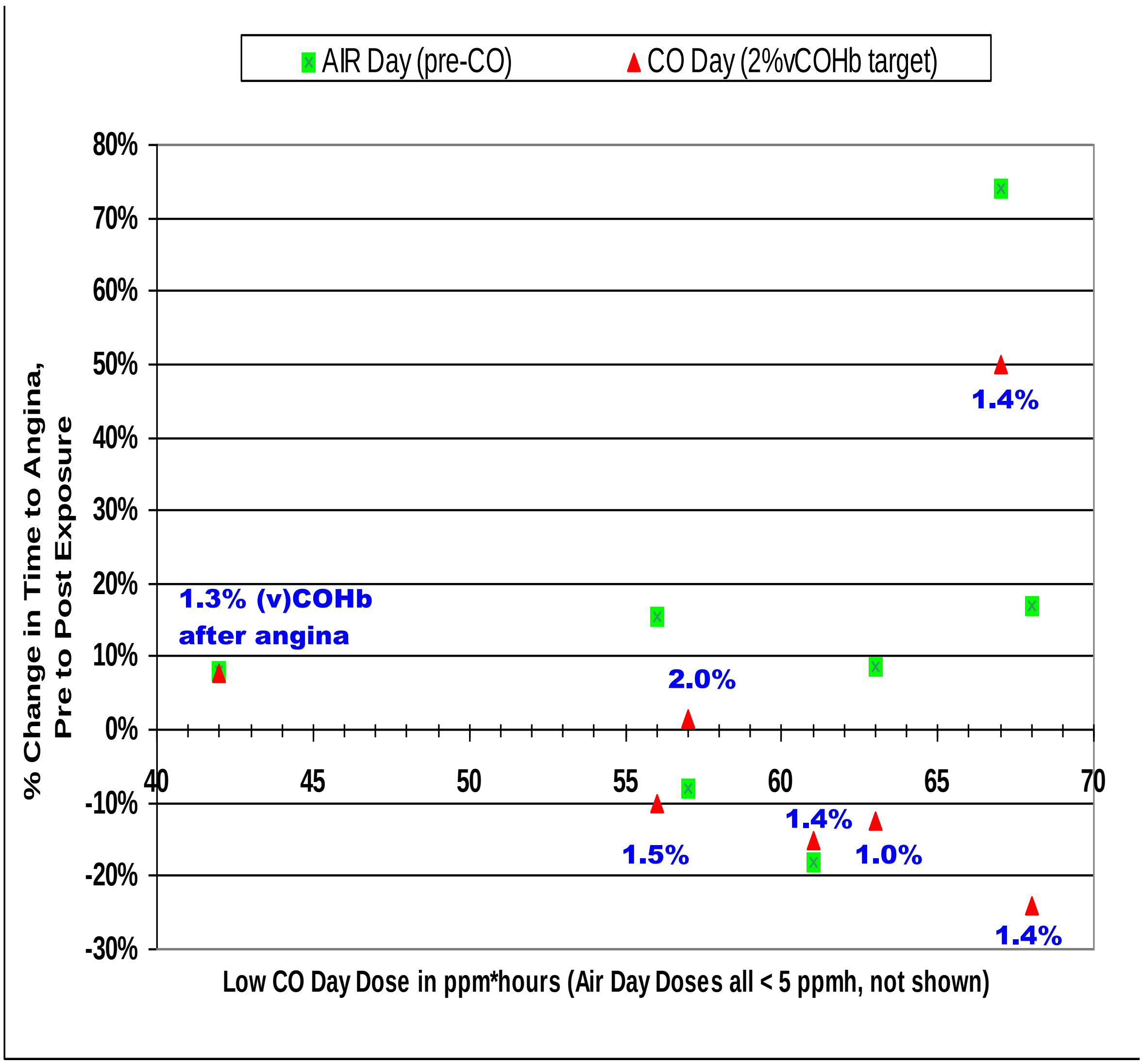
67. The ability of EPA's CO NAAQS to protect public health within an adequate margin of safety thus depends on whether any adverse health effects are significantly associated with CO exposures at doses of less than 72ppmh in any sensitive subpopulation.

68. The answer can be found in the Allred study's results. Seven of the subjects were so sensitive to CO that doses of just 42 to 68ppmh were sufficient to reach the targeted level on their low CO exposure day. Of these, four experienced significant declines in their same day time to angina (from 10.0% to 24.1%), one had no significant change, and two improved (7.6% and 23.3%) (Figure 4). When subtracted from their percent change in time to angina after exposure to air, the net decline among these men after CO exposure was 18.1%.

69. In contrast, the decline for all 63 subjects combined was only 4.2%, indicating that this group of the least exposed men did worse on average than all those exposed to higher doses.

70. Note also that all men in this group reached angina on the low CO day at or below EPA's 2% (v)COHb margin of safety. These anomalous findings should have been acknowledged and discussed in both the Allred study and EPA's NAAQS reviews of it. Even if the reasons for their hypersensitivity are unknown, they clearly represent a more sensitive population who are not protected by EPA's CO NAAQS.

Figure 4. Change in time to angina by CO dose and %(v)COHb for 7 subjects exposed at or below EPA's maximum allowable dose of 72ppmh and 2% (v)COHb margin of safety
Source: Allred data plotted by Donnay
Note 1: Inhaled CO doses on x-axis. Resulting %(v)COHb for each subject is shown in blue.



Controlled CO exposure studies cited by EPA as basis for CO NAAQS

71. EPA claims in its rulemaking that the CO NAAQS is based primarily upon the results of just one controlled CO exposure study that involved 63 men with coronary artery disease (CAD) and stable exertional angina (SEA). EPA further claims this study is supported by five smaller exposure studies involving similar subjects. The studies' key features are described below in Table 1.

Table 1. Controlled CO exposure studies cited by EPA as basis for CO NAAQS
Source: Compiled by Donnay from original sources

Author, Year (funder)	# CAD subjects by gender	CO ppm exposure level (with range if not fixed)	CO exposure duration	post-exposure (v)COHb mean by CO-oximetry	post-exposure (v)COHb range by CO-oximetry
Allred 1989a,b & 1991 (HEI)[14]	63 men	Low day= 117 (42-202) High day= 253 (143-357)	50 to 70 minutes	3.2% low CO5.6% high CO	not reported, but did report ranges post-exposure and post-exercise (Figure 2)
Adams, 1988 (UNC/EPA) [15]	22 men 8 women	100 and 200	approx 1 hour	5.2%	not reported
Anderson, 1973 (EPA) [16]	10 men	50 and 100	4 hours	2.9% low CO 4.5% high CO	(1.3 - 3.8) (2.8 - 5.4)
Kleinman, 1989 (CARB, HEI) [17]	26 men	100	1 hour	2.9%	(2.4 - 3.4)
Kleinman, 1998 (CARB) [18]	17 men	100	approx 2 hours	3.9% @sea 4.0% @altitude	(3.3 - 4.7) (3.2 – 4.9)

[14] Allred EN, Bleecker ER, Chaitman BR, Dahms TE, Gottlieb SO, Hackney JD, Hayes D, Pagano M, Selvester RH, Walden SM, et al. Acute effects of carbon monoxide exposure on individuals with coronary artery disease. Res Rep Health Eff Inst. 1989 Nov;(25):1-79.; Published simultaneously as Allred EN, Bleecker ER, Chaitman BR, Dahms TE, Gottlieb SO, Hackney JD, Pagano M, Selvester RH, Walden SM, Warren J. Short-term effects of carbon monoxide exposure on the exercise performance of subjects with coronary artery disease. N Engl J Med. 1989 Nov 23;321(21):1426-32. Erratum in: N Engl J Med 1990 Apr 5;322(14):1019; and again two years later as: Allred EN, Bleecker ER, Chaitman BR, Dahms TE, Gottlieb SO, Hackney JD, Pagano M, Selvester RH, Walden SM, Warren J. Effects of carbon monoxide on myocardial ischemia. Environ Health Perspect. 1991 Feb;91:89-132

[15] Adams KF, Koch G, Chatterjee B, Goldstein GM, O'Neil JJ, Bromberg PA, Sheps DS. Acute elevation of blood carboxyhemoglobin to 6% impairs exercise performance and aggravates symptoms in patients with ischemic heart disease. J Am Coll Cardiol. 1988 Oct;12(4):900-9.

[16] Anderson EW, Andelman RJ, Strauch JM, Fortuin NJ, Knelson JH. Effect of low-level carbon monoxide exposure on onset and duration of angina pectoris. A study in ten patients with ischemic heart disease. Ann Intern Med. 1973 Jul;79(1):46-50.

[17] Kleinman MT, Davidson DM, Vandagriff RB, Caiozzo VJ, Whittenberger JL. Effects of short-term exposure to carbon monoxide in subjects with coronary artery disease. Arch Environ Health. 1989 Nov-Dec;44(6):361-9.

Sheps, 1987 (UNC/EPA) [19]	25 men 5 women	100	approx 1 hour	3.6%	not reported

72. EPA states many other subpopulations may be susceptible to CO exposure, such as fetuses and people with respiratory diseases, but it insists that only for coronary artery disease specifically (and cardiovascular diseases more generally) is the scientific evidence of a causal link with CO sufficient to be considered as a basis for the CO NAAQS rulemaking.

73. In the more than 20 years since the Allred and other controlled exposure studies of CAD/SEA were published, however, EPA has not funded any controlled CO exposure studies of any other populations to investigate this.

74. The Allred study that EPA identifies as the primary basis of the CO NAAQS is known formally as the Health Effects Institute (HEI) Multi-center CO Study, and like of all HEI's air pollution research, it was jointly funded by EPA and motor vehicle manufacturers.

75. The Allred study was considered an impeccable effort at the time: designed by HEI's CO experts, co-authored by HEI's director of research, led by a distinguished team of cardiologists and statisticians from four universities including Harvard, overseen by two HEI committees while in progress and then reviewed by two more as well as HEI's board of directors when it was finished.

76. Its three clinical sites—but not HEI or the statistical center at Harvard—were also regularly audited regularly by an independent "Quality Assurance" team from A.D. Little, Inc. to ensure that the study's protocols were being rigorously followed and all data meticulously collected and preserved.

77. Although initially projected to take 3 years at a cost of $1 million, it eventually took six years and over $2.5 million to complete, making it the largest and most expensive CO study ever supported by EPA.

78. Unfortunately, HEI's executive director and the study's principal investigator (PI) acknowledged only in 2012—after the completion of EPA's CO rulemaking in 2011—that their separate archives of the study had both been discarded years ago and so were no longer available to EPA or the public for review. [20]

79. Ironically, when EPA commissioned the Allred study in 1983, it was based in part on what was then perceived as an urgent need to replicate the findings of a series of CO studies on which EPA had based its CO NAAQS up until that time.[21] Their validity was cast into doubt

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[18] Kleinman MT, Leaf DA, Kelly E, Caiozzo V, Osann K, O'Niell T. Urban angina in the mountains: effects of carbon monoxide and mild hypoxemia on subjects with chronic stable angina. Arch Environ Health. 1998 Nov-Dec;53(6):388-97.

[19] Sheps DS, Adams KF Jr, Bromberg PA, Goldstein GM, O'Neil JJ, Horstman D, Koch G. Lack of effect of low levels of carboxyhemoglobin on cardiovascular function in patients with ischemic heart disease. Arch Environ Health. 1987 Mar-Apr;42(2):108-16.

[20] Dr. Daniel Greenbaum (HEI) and Dr. Thomas Dahms.(Allred study PI), separately. 2011. personal communications.

[21] The Washington Post. EPA Probe Criticizes a Study Used in Air-Quality Standard Jun 7, 1983, pA17

by EPA's discovery that the researcher involved had been barred by both FDA and VA from doing any more human subjects research due to fraud.[22]

80. When an investigation launched by EPA discovered that this researcher had discarded all the records from all but one of his CO studies, EPA acknowledged that it could no longer cite any of his studies as the basis for the CO NAAQS.[23] Given that the Allred study data now also cannot be found or verified, EPA should not be permitted to continue basing the current CO NAAQS upon them.

81. All that remains of the Allred study are the methods and data as published in 1989 and 1991, along with descriptions of the study published elsewhere. The most informative is a 15-page "perspective" on the study published in HEI's first annual report in 1985, after the Allred study had already been underway for more than a year.[24]

82. This anonymous but apparently HEI-approved article includes a facsimile of the table of contents of the study's final protocol. [25] This shows the study started with three methods for measuring arterial COHb (with one specifically designated as the most accurate against with the other two were to be compared), two reference laboratories at different universities to check the reproducibility of each other's COHb methods (GC) as well as a less accurate COHb (COOx) method being used in the study's three clinical centers, and a pilot study involving healthy controls exposed to CO in the same fashion as the CAD cases with stable angina.

83. By the time the first version of the study was published in the NEJM, however, none of these features were even mentioned. The study was published without any mention of arterial COHb measurements, the third COHb method, the second reference lab, or any healthy controls.

84. Although appropriate scientific justifications may exist for all these changes, HEI's executive director and the principal investigator (PI) have been willing to provide any.[26]

85. According to the director of the second reference lab at Stanford University, Dr. Hendrik Vreman, his role in the study ended with a phone call from the project manager at HEI, Dr. Jane Warren. After months of unsuccessful efforts by both reference labs to replicate each others' results, she told him that the study team had decided to abandon the effort and finish the study with only the PI's reference lab.[27]

86. Any scientific study encountering such serious problems with its analytical methods should have disclosed this, of course, and more importantly, should not have continued unless and until it found a second reference lab that was capable of reproducing its results.

87. If HEI published results that it and the Allred study team knew could not be reliably reproduced and did not disclose this, or if they withheld critically important methods and findings, such as the results of the third COHb method, arterial COHb measurements, and

[22] The Washington Post. EPA Reviews Carbon Monoxide Data, May 5, 1983, pA25
[23] The Washington Post. Pollution Standard Has a Murky Past, Hearing Indicates. Oct 2, 1984, pA17
[24] Health Effects Inst. 1985. Annual Report. Cambridge MA: HEI
[25] ibid.
[26] Dr. Daniel Greenbaum and Dr. Thomas Dahms.(separately). 2011. personal communication
[27] Vreman H. 2012. personal communication.

healthy controls, any these actions alone would meet the definition of scientific misconduct promulgated by the federal Office of Research Integrity which also applies to EPA contractors.[28]

88. Even without such a formal finding, however, the fact that the authors made so many significant changes to their study protocol without disclosing them in their published reports is a very serious departure from the normal scientific method. These actions cast doubt on the integrity of the study and HEI's oversight of it, as well as EPA's oversight of HEI.

89. EPA cannot claim ignorance of these issues since it hired Dr. Ken Sexton, who had been HEI's director of Scientific Evaluation and Review while the Allred study was underway, to be EPA's Director of Science in 1987, just as the Allred study was concluding its clinical phase.[29]

90. Yet EPA has never explicitly acknowledged any weaknesses or limitations in the Allred study's design, methods or results. Neither do the Allred authors, which is extremely rare in the scientific literature.

91. EPA usually references all three published versions of the Allred study whenever it cites any one--as it does 8 times in the Integrated Science Assessment on CO, 18 in the Quantitative Risk and Exposure Assessment, 40 in the Policy Assessment and 14 in the final rule.[30] Since all three versions contain the same results, no added weight should be given to them.

92. The Allred study is actually less credible than most because the results from its three clinical centers did not correlate with each other, raising serious doubts about their relevance and reproducibility. As a committee of the National Research Committee wrote in a 2010 report for EPA on acute exposure guidelines: "At 2% COHb, the time to exercise induced angina was reduced by 4.2% in all patients (effects were significant in two test centers and non-significant in one center). At 4% COHb, the time was reduced by 7.1% in all patients (effects were significant in one, borderline significant in one and non-significant in one center)."[31]

93. Given that both EPA's CASAC CO Advisory Panel and many public comments urged EPA to abandon its scientifically unwarranted over-emphasis on the Allred study, EPA should have cited the Allred study only for historical purposes.

94. Neither should EPA have any confidence in the five other controlled CO exposure studies of men with CAD that it commonly quotes in support of the Allred study. Four of five used the same imprecise COOx instrument for measuring COHb (Figure 2 above), and three relied on the same "quality assurance program" led by the Allred study to check their calibration.[32] From a weight of the evidence perspective, these six studies are a far more "limited"—and now

[28] Withholding critical data and methods from publication are defined by the federal Office of Research Integrity, and by EPA as well, as a type of data falsification, which along with data fabrication and plagiarism are the primary forms of scientific misconduct that federal government agencies recognize.
[29] Ken Sexton. 2012. personal communication.
[30] EPA CO NAAQS documents accessed 3/21/12 at http://www.epa.gov/ttn/naaqs/standards/co/s_co_index.html
[31] National Research Council. 2010. Acute Exposure Guideline Levels for Selected Airborne Chemicals: Volume 8. Washington DC: National Academies Press
[32] Health Effects Institute. Annual Report. 1985 (FY84). Cambridge MA: HEI

also outdated—evidence base than all the thousands of CO studies published since using much more refined analytical methods.

95. As with all other EPA NAAQS rulemakings, the CO should be based on an unbiased reading and weighting of all the evidence and not primarily on any single study or group of studies, especially ones that can no longer be checked or reproduced. Institutional review boards in the modern era would never approve exposing angina subjects to such high CO exposures, in part because of the Allred study's widely cited results.

Relevance of CO doses and COHb levels reported in controlled exposure studies

96. EPA, the CO CASAC, and the National Research Council (in its review of the performance and effectiveness of the Health Effects Institute which EPA commissioned in 1991) have all noted the irrelevance for policy-making purposes of human studies involving exposures far above current regulatory limits.[33]

97. According to the NAS report, the CASAC even directed EPA not to include any such studies in future integrated science assessments written by EPA for NAAQS reviews.

98. In the 2000 edition of the CO ISA (then called a criteria document), even EPA finally acknowledged that "Human exposure studies conducted in the early 1980s and earlier distributions of COHb levels in the U.S. population that were relied on heavily in the previous assessment are no longer relevant to the current picture of ambient CO exposure in the 1990s."[34]

99. Based on its own advice, EPA should not have again cited Allred—or any of the five other CO exposure studies—as the basis for the latest CO NAAQS. All exposed their subjects to CO levels far above current standards, with most using fixed doses in the range of 50 to 400ppm for one and/or two hours.

100. To meaningfully evaluate the risks that people with CAD face from their actual CO exposures requires studies that can in real time and over many days measure individual CO exposures and cardiac function.

101. The first was published in February 2011 and, although too late then for inclusion in EPA's CO ISA, its findings are so significant that EPA should have considered them anyway during the public comment period.

102. Delfino et al. studied 38 elderly non-smoking men and women from two nursing homes with stable CAD and like the Allred population, no evidence of angina while at rest.[35] They measured all the NAAQS air pollutants just outside their nursing home over two five-day

[33] National Research Council. 1992. Structure and Performance of the Health Effects Institute. NRC: Washington DC [study sponsored by EPA and conducted by Commission on Life Sciences' Board on Environmental Studies and Toxicology]

[34] EPA. 2000. Air Quality Criteria for Carbon Monoxide (2000) Final Report. Washington, DC, EPA 600/P-99/001F

[35] Delfino RJ, Gillen DL, Tjoa T, Staimer N, Polidori A, Arhami M, Sioutas C, Longhurst J. Electrocardiographic ST-segment depression and exposure to traffic-related aerosols in elderly subjects with coronary artery disease. Environ Health Perspect. 2011 Feb;119(2):196-202.

periods while also monitoring the subjects' cardiac function around the clock.

103. The 1-hour CO exposures they recorded varied from 0.01ppm to 1.68ppm with a mean of 0.53ppm. Within this narrow range they found that each 0.42ppm increase in CO exposure was associated with very significant risks of ST segment depression that increased as the exposure time grew longer. Such a dose-response relationship is strong evidence of a causal effect.

104. After just one hour of increased exposure to an average of less than 0.5ppm, their risk of having a significant ST segment depression increased 28%, and by 8 hours it had doubled to 57%. Sixteen hours later, after 1 full day of elevated CO exposure, the risk of ST segment depression in these CAD patients had almost quadrupled to 207%. It then rose more slowly after 2 days to 222% and after 3 to 243%, at which point the total inhaled dose was still less than 0.5ppm*72 hours or 36ppmh.

105. If elevated CO exposure continued beyond 3 days, however, the ST risk gradually fell over several more days until returning to the original baseline level. This is presumably due to the subjects' gradually habituating to the new higher level of CO exposure, an effect that is well recognized in smokers. It is only the correlations of such high risks with such low doses that defies conventional explanation.

Environmental epidemiological studies on CO not considered by EPA

106. EPA's decision not to give any weight to evidence of adverse CO effects associated with the actual real world levels of exposure analyzed in EE studies runs directly counter to the explicit recommendations of the CO CASAC to place "greater emphasis on the findings of the epidemiologic studies versus the controlled clinical studies." [36]

107. The CO CASAC based its conclusions about EE studies on the fact that small increases in CO of one ppm or less are consistently associated with significantly increased risks of developing numerous medical conditions, being hospitalized for them, and even dying from them. The variety of adverse effects associated with CO exposure and the collective risk they pose to the American public is too great for EPA to ignore just because the pathways by which CO affects the body are not yet fully understood (Table 2).

Table 2. Adverse effects associated with CO in environmental epidemiology studies

Effects associated with CO exposure in fetuses, neonates, and children

FROM EE MORTALITY STUDIES
all causes among infants
all causes among first born children, post neo-natal
respiratory among infants and under 5 years old

[36] Brain JD, Samet JM. Letter to EPA Administrator Lisa P. Jackson. Review of the Policy Assessment for the Carbon Monoxide Primary National Ambient Air Quality Standards (NAAQS): External Review Draft. EPA-CASAC-10-013, June 8, 2010.

FROM EE BIRTH OUTCOME STUDIES
cardiac birth defects
low birth weight (full term)
small for gestational age birth weight
pre-term birth

FROM EE MORBIDITY STUDIES
elementary school absenteeism
acute respiratory illness among children
acute respiratory infections among school children
allergy symptoms among children
asthma symptoms, med use, prevalence among children
bronchitic symptoms among children
eczema among school children
respiratory symptoms among children
wheezing in infants

FROM EE HOSPITALIZATION STUDIES
asthma (combined hospitalizations and ER visits)
respiratory among neonates
respiratory among children under 15 years

FROM EE EMERGENCY ROOM VISIT STUDIES
asthma among children (and higher than for adults)
gastro-enteric disorders among children under 3 years
otitis media among children under 4 years
wheezing among children under 3 years
wheezing among adolescents

<u>Effects associated with CO exposure in adults</u>

FROM EE MORTALITY STUDIES
all non-accidental causes, daily
among cohort with congestive heart failure
among elderly vs non-elderly
among MI survivors
cardiac and respiratory causes combined
cardiovascular, including myocardial infarction (MI)
cardiovascular, first MI specifically
cerebrovascular (including all stroke)
coronary outside hospital
chronic obstructive pulmonary disease (COPD)
diabetes
pneumonia
SARS case fatality rate

FROM EE MORBIDITY STUDIES
asthma (severity, symptoms, medication use)
disability days

eczema
female lung cancer
hay fever symptoms
schizophrenia
sinusitis symptoms

FROM EE HOSPITALIZATION STUDIES
all causes
all respiratory/pulmonary causes
appendicitis
asthma
cardiovascular disease
cerebrovascular disease
COPD
epilepsy
headache
heart attack
ischemic heart disease
pneumonia
stroke

EMERGENCY ROOM VISIT STUDIES
all respiratory causes
asthma
COPD
depression
headache
heart failure
MI and angina
stroke
suicide attempts

CLINIC VISIT STUDIES
acute respiratory illnesses
lower respiratory tract illness

108. While EPA is correct in noting that most of these studies assess only ambient CO doses and not individual CO exposure levels, this does not negate their results. Whatever the strengths and weaknesses of EE studies, the risks they quantify can be meaningfully compared on the same scale in order to see which populations are most at risk from any given increase in CO exposure.

109. Such a comparison is given below. This sample of studies illustrates that fetuses and neonates consistently face the highest risks from each 1ppm (or less) increase in ambient CO exposure relative to 1.0, followed by children and then adults (Table 3). This is as expected given their relative smaller body sizes and faster growth rates.

110. The inappropriateness of EPA's choice of adults with angina as the most sensitive CO population on which to base the CO NAAQS is clear from the last place ranking of angina among all the various risks that have been associated with CO in EE studies. The increased risk of hospitalization for potentially fatal angina is less than 1% per ppm or less increase in CO.

111. In comparison, the highest increased risk reported for fetuses (per ppm or less increase in CO) is 195% for a cardiac birth defect that may be fatal if not surgically corrected.

Table 3: Magnitude of CO-related risks from selected epidemiology studies

Note 1: All risks are statistically significant at p<.05 with confidence intervals entirely above 1.0
Note 2 Adverse Effects= CBD:cardiac birth defects, D:deaths,
ER:emergency room visits, H:hospitalizations, P:prevalence
Note 3: RR= Relative Risk= increased risk of effect associated with exposure;
OR= Odds Ratio= ratio of odds of an effect in an exposed group vs unexposed group
Note 4: IQR= interquartile range of exposures, which spans middle two quartiles of distribution.

Adverse Effects associated with CO exposure in Fetuses, Children and Adults [1]	Significant Risk Effect Sizes in descending order [2, 3]	Unit of risk = ppm or IQR increase in exposure [4]	CO exposure time frame and # lag days to max risk if any	First Author, year
FETUSES				
CBD: ventricular septal defects	OR= 2.95 @> 2.4ppm OR= 2.09 @> 1.6ppm OR= 1.62 @> 1.1ppm	IQR 2, 3 and 4 compared to IQR1@<1.1ppm	daily average (avg) during 2nd month	Ritz, 2002[37]
D: respiratory mortality , all causes, up to 3 months	OR= 2.81 @ > 2ppm OR= 1.67 @ > 1ppm OR= 1.36 for all CO	1 ppm	2 week prior avg	Ritz 2006[38]
CBD: Tetralogy of Fallot	OR= 2.04 @> 0.7ppm (dose response at lower levels but n.s.)	IQR 2, 3 and 4 compared to IQR1@<0.7ppm	weeks 3 to 8	Gilboa 2005[39]
P: low birth weight	OR= 1.75 black OR= 1.31 all	IQR=1.1 ppm	3rd trimester	Maisonet 2001[40]
P: low birth weight	OR= 1.36	>75th percentile exposure	3rd trimester	Wilhelm 2005[41]
P: pre-term birth	OR= 1.27	>75th percentile	3rd trimester	Wilhelm 2005[42]

[37] Ritz B, Yu F, Fruin S, Chapa G, Shaw GM, Harris JA. Ambient air pollution and risk of birth defects in Southern California. Am J Epidemiol. 2002 Jan 1;155(1):17-25California. Am J Epidemiol. 2002 Jan 1;155(1):17-25.
[38] Ritz B, Wilhelm M, Zhao Y. Air pollution and infant death in southern California, 1989-2000. Pediatrics. 2006 Aug;118(2):493-502.
[39] Gilboa SM, Mendola P, Olshan AF, Langlois PH, Savitz DA, Loomis D, Herring AH, Fixler DE. Relation between ambient air quality and selected birth defects, seven county study, Texas, 1997-2000. Am J Epidemiol. 2005 Aug 1;162(3):238-52.
[40] Maisonet M, Bush TJ, Correa A, Jaakkola JJ. Relation between ambient air pollution and low birth weight in the Northeastern United States. Environ Health Perspect. 2001 Jun;109 Suppl 3:351-6.
[41] Wilhelm M, Ritz B. Local variations in CO and particulate air pollution and adverse birth outcomes in Los Angeles County, California, USA. Environ Health Perspect. 2005 Sep;113(9):1212-21.
[42] Id.

		exposure		
CHILDREN				
rhinoconjunctivitis rhinitis eczema	OR= 1.76 OR= 1.65 OR= 1.55	IQR<1 ppm	annual avg	Arnedo-Pena 2009[43]
daily asthma symptoms	OR= 1.31	1 ppm	1 day lag	Yu 2000[44]
H: asthma	RR= 1.19	IQR=1 ppm	0-5 day lags	Lee 2002[45]
H: asthma (0-14yr)	RR= 1.082, only CO significant	IQR=1.2 ppm	1 day lag	Fusco 2001[46]
ADULTS				
P: lung cancer in women	OR=1.38 @>0.82ppm OR=1.20 @>0.67ppm	Inter-tertile range	annual avg of all daily max 8h avg	Liu 2008[47]
H: appendicitis	OR= 1.35 in summer OR= 1.06 annually	IQR	5 day lag	Kaplan 2009[48]
H: stroke	RR= 1.107, warm days only	IQR<1 ppm	3 day lag	Kettunen 2007[49]
D: non-traumatic mortality	RR= 1.086 if >65 yrs RR= 1.041 if <65 yrs	1.29 ppm	1 day lag	Cakmak,2007[50]
D: cardiovascular	RR= 1.07	0.2 ppm	2 day lag	Lin 2009[51]
D: congestive heart failure	RR= 1.065	IQR=2 ppm	same day	Burnett 1997[52]
D: ischemic stroke mortality	RR= 1.06	IQR=1 ppm	1 day lag	Hong 2002[53]

[43] Arnedo-Pena A, García-Marcos L, Carvajal Urueña I, Busquets Monge R, Morales Suárez-Varela M, Miner Canflanca I, Batlles Garrido J, Blanco Quirós A, López-Silvarrey Varela A, García Hernández G, Aguinaga Ontoso I, González Díaz C. [Air pollution and recent symptoms of asthma, allergic rhinitis, and atopic eczema in schoolchildren aged between 6 and 7 years]. Arch Bronconeumol. 2009 May;45(5):224-9. Epub 2009 Apr 16.
[44] Yu O, Sheppard L, Lumley T, Koenig JQ, Shapiro GG. Effects of ambient air pollution on symptoms of asthma in Seattle-area children enrolled in the CAMP study. Environ Health Perspect. 2000 Dec;108(12):1209-14.
[45] Lee JT, Kim H, Song H, Hong YC, Cho YS, Shin SY, Hyun YJ, Kim YS. Air pollution and asthma among children in Seoul, Korea. Epidemiology. 2002 Jul;13(4):481-4.
[46] Fusco D, Forastiere F, Michelozzi P, Spadea T, Ostro B, Arcà M, Perucci CA.Air pollution and hospital admissions for respiratory conditions in Rome, Italy. Eur Respir J. 2001 Jun;17(6):1143-50.
[47] Liu CC, Tsai SS, Chiu HF, Wu TN, Yang CY. Ambient exposure to criteria air pollutants and female lung cancer in Taiwan. Inhal Toxicol. 2008 Feb;20(3):311-7.
[48] Kaplan GG, Dixon E, Panaccione R, Fong A, Chen L, Szyszkowicz M, Wheeler A, MacLean A, Buie WD, Leung T, Heitman SJ, Villeneuve PJ. Effect of ambient air pollution on the incidence of appendicitis. CMAJ. 2009 Oct 27;181(9):591-7.
[49] Kettunen J, Lanki T, Tiittanen P, Aalto PP, Koskentalo T, Kulmala M, Salomaa V, Pekkanen J. Associations of fine and ultrafine particulate air pollution with stroke mortality in an area of low air pollution levels. Stroke. 2007 Mar;38(3):918-22.
[50] Cakmak S, Dales RE, Vidal CB. Air pollution and mortality in Chile: susceptibility among the elderly. Environ Health Perspect. 2007 Apr;115(4):524-7. Epub 2007 Jan 8.
[51] Lin CM, Liao CM. Temperature-dependent association between mortality rate and carbon monoxide level in a subtropical city: Kaohsiung, Taiwan. Int J Environ Health Res. 2009 Jun;19(3):163-74.
[52] Burnett RT, Dales RE, Brook JR, Raizenne ME, Krewski D. Association between ambient carbon monoxide levels and hospitalizations for congestive heart failure in the elderly in 10 Canadian cities. Epidemiology. 1997 Mar;8(2):162-7.
[53] Ha EH, Hong YC, Lee BE, Woo BH, Schwartz J, Christiani DC. Is air pollution a risk factor for low birth weight in Seoul? Epidemiology. 2001 Nov;12(6):643-8.

H: heart attack	RR= 1.056	1 ppm	same day	Zanobetti 2006[54]
H: pneumonia	RR= 1.055	1 ppm	same day	Zanobetti 2006[55]
H: all cardiovascular among adults over 65	RR= 1.055	1 ppm	same day 1hr max	Bell 2010[56]
H: congestive heart failure	RR= 1.052	0.55 ppm	24hr avg	Wellenius2005 [57]
H: asthma (all ages)	RR= 1.048, only CO significant	IQR=1.2 ppm	same day	Fusco 2001[58]
H: COPD	RR= 1.043, only CO significant	IQR=1.2 ppm	same day	Fusco 2001[59]
D: heart attack mortality	RR= 1.038	0.2 ppm	0-4 day lag	Berglind 2009[60]
H: Ischemic heart disease	RR= 1.014 over 65yrs	1 ppm	2 day lag	Lee 2003[61]
H: angina	RR= 1.009, only CO significant	<1 ppm, range =1.34-46.9, mean=8.8	1 day lag	Hosseinpoor 2005[62]

112. These studies together document that the adverse effects associated with small increases in ambient CO exposure are significant and affect all age groups although they may peak over different time frames and vary by two orders of magnitude from the most sensitive to least. Clearly, CO effects cannot be completely characterized by any single study or even any group of studies focused on just one population at risk or one outcome.

113. While EPA acknowledges the significance of “the now much-expanded epidemiological evidence base, which is coherent with the evidence from these [older controlled human exposure] studies” linking coronary artery disease with CO exposure. EPA’s REA concluded that “CO associations [with CAD] generally remain robust in co-pollutant models, that the

[54] Zanobetti A, Schwartz J. Air pollution and emergency admissions in Boston, MA. J Epidemiol Community Health. 2006 Oct;60(10):890-5.
[55] Id.
[56] Bell ML, Peng RD, Dominici F, Samet JM. Emergency hospital admissions for cardiovascular diseases and ambient levels of carbon monoxide: results for 126 United States urban counties, 1999-2005. Circulation. 2009 Sep 15;120(11):949-55. Epub 2009 Aug 31.
[57] Wellenius GA, Bateson TF, , Mittleman MA, Schwartz J. Particulate air pollution and the rate of hospitalization for congestive heart failure among medicare beneficiaries in Pittsburgh, Pennsylvania. Am J Epidemiol. 2005 Jun 1:161(11) 1030-6.
[58] Fusco D, Forastiere F, Michelozzi P, Spadea T, Ostro B, Arcà M, Perucci CA.Air pollution and hospital admissions for respiratory conditions in Rome, Italy. Eur Respir J. 2001 Jun;17(6):1143-50.
[59] Id.
[60] Berglind N, Bellander T, Forastiere F, von Klot S, Aalto P, Elosua R, Kulmala M, Lanki T, Löwel H, Peters A, Picciotto S, Salomaa V, Stafoggia M, Sunyer J, Nyberg F; HEAPSS Study Group. Ambient air pollution and daily mortality among survivors of myocardial infarction. Epidemiology. 2009 Jan;20(1):110-8.
[61] Lee JT, Kim H, Cho YS, Hong YC, Ha EH, Park H. Air pollution and hospital admissions for ischemic heart diseases among individuals 64+ years of age residing in Seoul, Korea. Arch Environ Health. 2003(b) Oct;58(10):617-23.
[62] Hosseinpoor AR, Forouzanfar MH, Yunesian M, Asghari F, Naieni KH, Farhood D.Air pollution and hospitalization due to angina pectoris in Tehran, Iran: a time-series study. Environ Res. 2005 Sep;99(1):126-31.

specific endpoints are coherent with human clinical and toxicologic evidence from studies conducted at higher concentrations, and that these considerations 'support a direct effect of short-term CO exposure on cardiovascular morbidity at ambient concentrations below the current NAAQS level.'"[63]

114. EPA at least reviewed some EE studies in its ISA on CO. It failed to consider at least 46 more EE studies submitted during the public comment period.

115. Therefore, there is no credible scientific justification for EPA to then conclude that no EE studies of any kind should be given any weight in formulating the CO NAAQS. This decision runs counter to EPA's reliance on the same types of studies, including many by the same authors from the same datasets, in other recent NAAQS rulemakings related to particulates, nitrogen dioxide and sulfur dioxide.

116. Most significant is EPA's refusal to give any weight to the first nationwide CO study of hospitalizations for cardiovascular diseases which examined the records of over 9.3 million Medicare enrollees in 126 US urban counties from 1999 to 2005.[64]

117. The study was funded by EPA and co-authored by Dr. Samet, chair of EPA's CASAC, and submitted for publication in January 2009, before the May 2009 deadline set by EPA for the inclusion of new research in the CO NAAQS. Although not published until August 2009, the CO CASAC was still empaneled, meeting, and making recommendations to EPA under Dr. Samet's leadership until at least June 10, 2010, when he and Dr. Brain, the chair of the CO advisory panel, sent EPA comments on the draft PA.[65]

118. There is no evidence in the CO CASAC's consensus letters or the comments of individual members that this study was ever considered or brought to EPA's attention. But its conclusions should have been.

119. Dr. Samet and his co-authors wrote that "We found evidence of an association between short-term exposure to ambient CO and risk of CVD hospitalizations, even at levels well below current US health-based regulatory standards. This evidence indicates that exposure to current CO levels may still pose a public health threat, particularly for persons with CVD."[66]

120. The "positive and statistically significant association" they found with same-day increases in CO was not for transient angina but for many much more serious adverse effects, including hospitalization for ischemic heart disease, heart rhythm disturbances, heart failure, cerebrovascular disease, and cardiovascular (CVD) admissions overall.

[63] US EPA 2009. Carbon Monoxide National Ambient Air Quality Standards: Scope and Methods Plan for Health Risk and Exposure Assessment, US EPA, Washington, DC, EPA-452/R-09-004. (quoting US. EPA. Integrated Science Assessment for Carbon Monoxide, US EPA, Washington, DC, EPA/600/R-09/019F, 2010).
[64] Bell ML, Peng RD, Dominici F, Samet JM. Emergency hospital admissions for cardiovascular diseases and ambient levels of carbon monoxide: results for 126 United States urban counties, 1999-2005. Circulation. 2009 Sep 15;120(11):949-55. Epub 2009 Aug 31.
[65] Brain J, Samet J. Letter to Lisa Jackson, EPA, June 8, 2010. Note the CO CASAC never met to discuss the proposed CO rule and never sent EPA a final closure letter.
[66] Bell ML, Peng RD, Dominici F, Samet JM. Emergency hospital admissions for cardiovascular diseases and ambient levels of carbon monoxide: results for 126 United States urban counties, 1999-2005. Circulation. 2009 Sep 15;120(11):949-55. Epub 2009 Aug 31.

121. Even after adjusting for potentially confounding pollutants, a significant risk persisted, and even started at levels below 1ppm. They reported that each 1-ppm increase in the same-day daily 1-hour maximum CO level was associated with a 0.55% increase in hospitalizations for CVD, and with a very tight 95% confidence interval of just 0.36% to 0.74%.

122. While there is continuing scientific uncertainty regarding the exact mechanisms by which CO may be producing such serious adverse effects even at ambient levels below 1ppm, the authors concluded that their results "were consistent with clinical and animal model studies finding that CO exposure can adversely affect cardiac function"—although clearly not related to any significant increases in %(v)COHb.

123. Given that EPA has lowered other air quality standards to protect public health from risks posed by other NAAQS pollutants based on the same type of EE evidence, it should now promptly do so for CO as well even if the risks are "not precisely identified as to nature or degree."[67]

124. The fact that EE studies are designed to quantify the risks of adverse effects occurring in large populations that are associated with small increases in ambient pollutants should give them much more, and not less, weight in EPA's assessment of the current CO NAAQS and its ability to protect public health with a reasonable margin of safety.

125. This type of risk assessment cannot be made based on the Allred or any other controlled exposure studies, because the subjects were not randomly selected and so are not representative of any larger population except perhaps the three cardiology clinics from which they were recruited.

126. To be consistent, EPA should have rated all available CO-related EE studies according to the "General Criteria for Study Selection" in its Integrated Review Plan for CO (see Table 4 below at 150*)* before deciding which ones were most worthy of inclusion.

<u>Poisoning studies on CO not considered by EPA</u>

127. EPA claims that the 156 CO poisoning studies (EPA-HQ-OAR-2008-0015-0179 at 17-27) submitted by the public should not be considered in reviewing the CO NAAQS because they involve CO exposures and doses over time that greatly exceed those of regulatory relevance.

128. Yet all of the exposure levels and most of the inhaled doses used in the Allred study upon which EPA primarily relies were greater than the current 1-hour average exposure limit of 35ppm.

129. The exposure levels ranged from 42ppm to 357ppm, which at the high end is more than 10 times the highest average exposure allowed by EPA's 1-hour CO NAAQS, and over 100 times more than the current national outdoor average of ambient CO.

[67] US EPA. 2011. National Ambient Air Quality Standards for Carbon Monoxide (proposed rule). 40 CFR Parts 50, 53 and 58 Federal Register, 76(29), 2/11/11, 8158-8220. EPA–HQ–OAR–2008–0015 and FRL–9261–4; 2060–AI43. Accessed 4/4/11 at http://govpulse.us/entries/2011/02/11/2011-2404/national-ambient-air-quality-standards-for-carbon-monoxide#id772766

130. If EPA's policy is actually to exclude all CO poisoning studies from consideration for this reason, it should be consistent and also exclude all other CO studies that involved higher than ambient levels of exposure, as the CASAC has previously recommended, including the Allred study.[68]

131. Commenters pointed to several important reasons for EPA to consider all studies of CO poisoning, however. Most important is that adverse effects documented from exposures to very high levels of CO lend biological plausibility to reports of similar effects seen at much lower levels of exposure in EE studies.

132. Case studies of CO poisoning that report on multiple individuals also can provide important evidence of differences in susceptibility among men vs women and children vs the elderly. They may also identify various risk and protective factors of relevance to ambient exposures.

Literature reviews on CO not considered by EPA

133. EPA claims that it would not be appropriate to consider the 143 review articles about CO submitted by the public. (EPA-HQ-OAR-2008-0015-0179 at 31-40) Presumably this is because EPA recognizes that review articles do not always accurately or fully report the results of the studies they cite. But the same may be true of any single study, and it is impossible for any reviewer to know this unless and until they actually read not just the abstract but the entire article.

134. The list of CO studies referenced in the ISA nevertheless includes many independent review articles as well as ones written by EPA staff in peer-reviewed journals and the ISA itself.

135. Review articles obviously serve a useful purpose in summarizing and synthesizing the results of many related studies, especially in rapidly growing areas of CO research such as that related to endogenous CO (produced by all humans from the breakdown of heme proteins) and CO-related genetics.

136. Among the topics covered in just one of these reviews are the roles of endogenous CO—at subambient concentrations—in vascular tone, atherosclerosis, pregnancy, reproductive hormones, male reproductive function, liver function, stress response, nerve transmission in the brain, and immune response.[69]

137. The authors conclude that "there is now ample evidence that CO is a vital molecule in human health and disease. Every passing week brings new knowledge about the systems in which CO acts and the mechanisms by which it performs its myriad functions. Although the toxicological effects of high concentrations of exogenous CO fueled most of the research for nearly a century, observations over the last decade of the effects of lower concentrations have led to a remarkable rehabilitation of this gas, from poison to physiological effector and, perhaps, pharmacological agent."

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[68] CASAC recommendation is cited by US General Accounting Office. 1986. Air Quality Standards: The role of the Health Effects Institute in conducting research. 86-177BR

[69] Morse D, Sethi J. Carbon monoxide and human disease. Antioxid Redox Signal. 2002 Apr;4(2):331-8.

138. Over 1,400 articles were published on endogenous carbon monoxide by 2009 when EPA's ISA was completed, yet EPA says this evidence is too "limited" to consider given the lack of data on how inhaled CO may interact with CO within the body.

139. Most studies of endogenous CO pathways start by exposing animals or humans to various relatively low doses of CO, CO precursors, or CO agonists and then studying how endogenous pathways are affected by these exposures at the molecular level. This is exactly the information EPA should have reviewed to learn how low doses of inhaled CO affect human health.

140. This broader 21st century perspective of CO is missing from EPA's CO NAAQS review, which incorrectly claims ambient CO has no clearly established effects on or interaction with endogenous CO once inhaled.

141. EPA's decision to exclude only review articles submitted by the public appears arbitrary and capricious. Unless EPA is willing to exclude all reviews including those by EPA staff from consideration in NAAQS rulemakings, it should include them all, and especially those that review the effects of CO doses at levels of regulatory significance (i.e. below 35ppmh-72ppmh).

Studies on CO submitted by public that EPA claims it reviewed

142. There are almost 100 more CO studies submitted in public comment that EPA claims it considered in the CO NAAQS review but which are not listed in the ISA and not discussed or cited in any of EPA's other CO NAAQS review documents.

143. Since EPA did not cite any of these studies as either supporting or not supporting its proposed CO rule, it appears that EPA staff contractors either:

a) did not actually review any of these studies, or
b) reviewed them but found no evidence of adverse CO effects of sufficient relevance to public health to merit inclusion in the ISA or consideration in the CO NAAQS rulemaking.

144. Had EPA found any such evidence in any of these studies, it should have been included in the ISA. Much more likely is that EPA staff and contractors never considered them. If they had, they should have at least deleted the seven CO reviews and nine reports of CO poisoning that are still on the list, in keeping with EPA's policies regarding the *a priori* exclusion of these types of research from the CO NAAQS review.

145. In total EPA failed to address 393 studies (see Attachment A) on the health effects of CO submitted by myself and other commenters, which as expressed in the previous three sections and in their respective comments are extremely relevant to the CO NAAQS.

<u>EPA's Integrated Review Plan for CO</u>

146. EPA finished its Integrated Review Plan (IRP) for the CO NAAQS review in 2008, after soliciting comments from the public and the CO CASAC.[70] According to this plan, the CO NAAQS review was supposed to begin with the compilation of a comprehensive list of all peer-reviewed CO literature published since EPA's completion of the last criteria document on CO in 2000:[71]

147. The IRP committed EPA to a follow a detailed procedure:

"An initial publication database will be established by searching the online databases MEDLINE, ISI Web of Knowledge, Toxfile, Pascal, Biosis, and Embase using as key words terms including carbon monoxide, methane, carbon dioxide, CO, CH4, CO2, hydroxyl radical, carboxyhemoglobin, COHb, hypoxia, traffic, and combustion. Targeted searches will also be conducted to identify articles relevant to specific health, ecological, and physical science disciplines. As appropriate, the search strategies will be periodically reexamined and modified to enhance identification of pertinent published papers. Additional papers will be identified for inclusion in the publication base in several ways. These include the review of pre-publication tables of contents for journals in which relevant papers may be published, as well as independent identification of relevant literature by expert authors. In addition, publications that may be pertinent are identified by both the public and CASAC during the external review process. The studies identified will include research published or accepted for publication by a date determined to be as inclusive as possible given the relevant target dates in the NAAQS review schedule. Some additional studies, published after that date, may also be included if they provide new information that impacts one or more key scientific issues. The combination of these approaches should produce the comprehensive collection of potentially pertinent studies needed to form the basis of the ISA."

148. EPA's determination regarding the sufficiency of the CO NAAQS should have been based on consideration of all peer-reviewed CO studies published since the last review was completed. But as discussed below, EPA's efforts in this regard were undermined by failure of its staff and/or contractors to consider all or even one tenth of the peer-reviewed literature published on CO since EPA completed the last CO NAAQS review.[72].

149. Per EPA's IRP, each study so identified was then supposed to be assessed according to seven specific criteria to determine whether it should be included in the ISA (Table 4):

150. "Consideration of these issues," claimed EPA, "… informs our judgments on the relative quality of individual studies and allows us to focus the assessment on the most pertinent studies."

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[70] EPA. 2008. Plan for Review of the National Ambient Air Quality Standards for Carbon Monoxide. Washington DC: EPA-452/R-08-005.
[71] EPA 2000. Air Quality Criteria for Carbon Monoxide (2000) Final Report. Washington DC: EPA 600/P-99/001F
[72] EPA 2010. Integrated Science Assessment on Carbon Monoxide. Washington DC: EPA/600/R-09/019F. This lists 817 references in total but over 7,000 peer-reviewed articles on CO were published from 2000 to 2009.

Table 4. "General Criteria for Study Selection" from EPA's Integrated Review Plan
Source: excerpted from EPA IRP on CO, 2008

a. "In assessing the scientific quality and relevance of epidemiological and human or animal toxicological studies, the following considerations will be taken into account.

(1) * To what extent are the aerometric data, exposure, or dose metrics of adequate quality and sufficiently representative of population exposure to serve as indicators of exposure to ambient CO?

(2) * Were the study populations adequately selected and are they sufficiently well defined to allow for meaningful, reliable comparisons between study groups?

(3) * Are the health endpoint measurements meaningful, reliable, and clinically significant?

(4) * Does the study contain unique data, such as the documentation of a previously unreported effect, documentation of the mechanism for an observed effect, or information on exposure-response relationships?

(5) * Are the statistical analyses appropriate, properly performed, and properly interpreted with sufficient statistical power?

(6) * Are likely covariates (i.e., potential confounders or effect modifiers) adequately controlled or taken into account in the study design and statistical analysis?

(7) * Are the reported findings internally consistent, biologically plausible, and coherent in terms of consistency with other known facts?

151. While this plan appears sound, EPA cannot provide any list of CO references that its staff and/or contractors compiled and considered for the CO ISA. Whatever the process, the result was an ISA on CO that contains only 817 references of any kind, many of which are unrelated to CO or published before the last review in 2000.

152. In contrast, the PubMed database maintained by the National Library of Medicine lists 7,849 peer-reviewed articles on CO published in English from 2000 through 2009. Admittedly, not all of these CO studies are relevant to the CO NAAQS, but unless EPA staff or its contractors read them, there is no way they could be sure they were including all those that scored well on the "General Criteria for Study Selection" and excluding those that did not.

153. At whatever point EPA realized its published IRP was not being followed, it should have suspended the process of compiling CO literature and issued a new plan for public and CASAC comment before continuing, or it should have started the process over and followed the original plan.

CO NAAQS ranges recommended by EPA staff and CO CASAC

154. Both EPA staff and the CO CASAC recommended that the Administrator consider lower ranges for both the 1-hour and 8-hour standards (Table 5). The CO CASAC expressed a "preference for a lower standard"[73] and in its comments on the draft Policy Assessment on CO specifically urged the EPA to consider revising the 8-hour CO standard "to levels within the range of 3 to 6ppm, with no more than a single exceedance, or revise the form of the standard to 99th percentile with a concentration range of 3-5ppm."

Table 5. Current and proposed ranges for CO NAAQS
Source: EPA 2010[74]

		1-hr avg CO	8-hr avg CO
Current CO NAAQS:	i.	35ppm	9ppm, max dose=72ppmh
Ranges per EPA staff: (all 99th percentile form, averaged over 3 years)			
	ii.	5-8ppm (low)	3-4ppm, max dose 24-32ppmh
	iii.	9-10ppm (med)	5-7ppm, max dose 40-56ppmh
	iv.	11-15ppm (high)	8-9ppm, max dose 64-72ppmh
Lowest range per CASAC:			
	v.	5-15ppm	3-5ppm (99th percentile form), max dose= 24-40ppmh
	vi.	5-15ppm	3-6ppm (single exceedance), max dose=24-48ppmh

155. With regard to the 1-hour standard, CO CASAC said the EPA should consider "a range of concentrations from 5ppm to 15ppm, combined with a 99th percentile or fourth highest daily maximum."[75] In response, EPA's final Policy Assessment on CO proposed three such ranges for each standard, although only the lowest was within the limits recommended by CO CASAC

156. Although the proposed ranges are much lower than the current CO NAAQS allows, they are still too high to have any impact on current ambient ranges.

157. If they were actually meant to protect public health from the many risks associated with ppm or less increases in CO, the new 8-hour standard would have to be set below 1ppm (at which point EPA should switch to regulating CO in parts per billion, as EPA has long done for the other gas NAAQS).

158. Instead, the lowest ranges proposed by both EPA staff and the CO CASAC are just above the current national 1-hour and 8-hour national maximum averages.

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[73] Brain JD, Samet JM. Letter to EPA Administrator Lisa P. Jackson. Review of the Policy Assessment for the Carbon Monoxide Primary National Ambient Air Quality Standards: External Review Draft. EPA-CASAC-10-013, June 8,2010

[74] US EPA. Policy Assessment for the Review of the Carbon Monoxide National Ambient Air Quality Standards. October 2010. EPA 452/R-10-007

[75] Brain JD, Samet JM. Letter to EPA Administrator Lisa P. Jackson. Review of the Policy Assessment for the Carbon Monoxide Primary National Ambient Air Quality Standards: External Review Draft. EPA-CASAC-10-013, June 8, 2010

159. While they represent the largest percent reductions ever proposed by EPA or any CASAC committee for any NAAQS rulemaking—as much as 83% lower for the 1-hour standard and 66% for the 8-hour—they would not require any significant further reductions in CO emissions and so would do nothing to prevent or reduce all the CO risks that Americans face from small increases of 1ppm or less within current ambient ranges.

160. They would nevertheless be an improvement over the current standard as they would prevent major CO sources from significantly increasing their emissions within the currently allowed "margin of pollution" up to 9ppm.

161. As such, these alternative ranges should have at least been mentioned in EPA's proposed and final CO rule so that the public and CO CASAC could comment upon them. This has been EPA's normal procedure in other NAAQS rulemakings, but not this time.

162. Also unprecedented , to the best of my knowledge, was EPA's decision not to seek any further comments from the CO CASAC after the proposed rule was published.

<u>EPA's misinterpretation of WHO, ATSDR and NRC/BEST recommendations</u>

163. In EPA's reply to public comments, EPA dismisses as inconsequential the published statements on CO by several highly respected scientific organizations. These groups—the World Health Organization (WHO), the Board on Environmental Studies and Toxicology of the National Research Council (NRC), and the US Agency for Toxic Substances and Disease Registry (ATSDR)—have all published reports saying no safe level of CO dose can be established or recommended.[76]

164. Their reasons vary but include the fact that controlled exposure studies of sensitive populations (including Allred) have established dose response relationships for adverse effects with no evidence of any threshold of either CO doses or %(v)COHb below which no adverse effects occur. Most importantly they noted that, given the many physiological roles of endogenous CO, any source of external CO exposure has the potential for producing potentially adverse effects.

165. EPA claims in response that based on the CO literature it reviewed, evidence of any significant interaction between inhaled CO and endogenous CO pathways is still "too limited" and/or "uncertain" to be relied upon in setting the CO NAAQS.

166. Although EPA acknowledges that "the data on which the NRC relied for their decisions was … focused on effects observed in response to elevations in COHb (e.g., Allred et al., 1989)," it nevertheless claims the NRC's decision not to recommend a safe level of CO exposure below which CO-sensitive populations will be protected is not "inconsistent with the Administrator's judgment as to the degree of protection afforded by the current standards."[77]

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[76] (WHO) Schwela D. Air pollution and health in urban areas. Rev Environ Health. 2000 Jan-Jun;15(1-2):13-42.
US ATSDR. Sept 2009 Toxicological Profile for Carbon Monoxide. CAS# 000630-08-0
National Academy of Sciences Committee on Acute Exposure Guideline Levels; Committee on Toxicology; National Research Council. 2010. Acute Exposure Guideline Levels for Selected Airborne Chemicals: Volume 8. Washington DC: National Academies Press

[77] EPA 2011. Responses to Significant Comments on the 2011 Proposed Rule on the National Ambient Air Quality Standards for Carbon Monoxide. February 11, 2011. 76 FR 8158

167. Absent any safe level of CO exposure below which the health of sensitive subpopulations can be protected, however, the only rational alternative is to promulgate CO standards that are "as low as reasonably achievable" in order to reduce the risks posed to sensitive subpopulations by CO exposures at any level.

168. The ALARA approach to the regulation of pollutants has been used by EPA repeatedly as the basis for non-NAAQS rulemakings (requiring new power plants to be built with the latest available pollution controls, for example, rather than limiting their emissions per se).

169. EPA even proposed but never adopted regulations in the 1970s that would have required automakers to recall and retrofit all vehicles more than 5 years old with the best catalytic converters then available in order to most quickly reduce ambient CO levels. (CO levels in urban areas were then several times higher than the CO NAAQS allowed.)

170. Forty years later, "mobile source" (vehicular) emissions still account for more than half of all ambient CO. These could be reduced to near zero, however, by the best catalytic converters now available, but EPA does not require their use. If EPA pursued the same ALARA regulatory strategy it proposed in the 1970s, CO emissions would have fallen more quickly then and would be much smaller now

Susceptibility of children

171. Environmental epidemiology (EE) studies document that the risks fetuses face for birth defects, low birth weight and preterm birth from small (less than 1ppm) increases maternal CO exposures are two orders of magnitude greater than those have been quantified for adults in other EE studies (Table 3 above).

172. Children are not as CO-sensitive as fetuses but they too face CO risks that are up to one order of magnitude greater than those facing adults.

173. EPA's ISA on CO devotes an entire section to studies documenting the association between low level CO exposure and various measures of asthma morbidity. It even concluded that the evidence is sufficient to be "suggestive of a causal relationship."

174. Yet EPA's Risk and Exposure Assessment, its Policy Assessment, proposed rule and final rule do not identify asthmatics of any age as a vulnerable population and none even include the word asthma. EPA should have acknowledged in its final rule that all asthmatics and especially children are more sensitive to CO than non-asthmatics.

175. Fetuses and neonates are at even greater risk for CO outcomes that affect only them, including birth defects, low birth weight and neonatal respiratory mortality, as discussed below and not refuted by EPA.

176. The largest effect sizes ever reported for CO exposure in any EE study for any outcome in any population are for birth defects. These clearly represent a more significant adverse event as defined by the CAA than the Allred study's focus on reductions in time to angina.

177. The effect sizes are consistently associated with CO even in multi-pollutant models that modify the results to account for interactive effects. Most significant are the odds ratios for developing cardiac ventricular septal (CVS) birth defects.

178. Compared to the lowest documented range of average maternal exposure in the second month of pregnancy (which are below 1.14ppm), the odds of having a child with CVS are 62% greater when the average maternal CO exposure in the second month of pregnancy is 1.14-1.57ppm; 109% greater from 1.58ppm to 2.39ppm, and 195% when above 2.39ppm.[78]

179. The largest risks reported for low birth weight are 31% for children of all races and 75% for black children. These were both associated with increases of less than 1.2ppm in outdoor average CO during various trimesters of pregnancy. [79]

180. The risk of neonatal respiratory mortality from CO exposure is greatest in the second month of life, at 36% per 1ppm increase in average exposure [80]. It gradually declines with age but still averages 15% up to age 5 [81].

181. Given that fetuses and children face higher relative risks for adverse effects associated with CO exposure than adults per each increment of additional exposure, they are also less protected than adults by CO NAAQS limits at any level.

182. The only way EPA can protect children from CO risks is to establish a standard that is designed to be protective of their greater sensitivity to CO.

183. Since controlled CO exposure studies of fetuses, infants and children would be unethical, these types of EE studies are the only type of scientific studies that EPA can rely upon to assess the effectiveness of its CO NAAQS at protecting more sensitive populations.

184. If EPA's CO NAAQS were actually effective at protecting public health with an adequate margin of safety, none of the EE studies should have been able to detect any significantly increased risks for any type of morbidity or mortality in any subpopulation associated with any duration of any exposure to any CO levels at or below 9ppm average for 8 hours.

Consequences of maintaining CO NAAQS at 1971 level

185. The gradual decline in ambient CO over the last 20 years is due to a gradual decline in the amount of CO emissions from on-road vehicles, but these still account for more than 60% of the total. This has been driven entirely by other EPA standards concerning catalytic converters and auto emissions, while CO emissions from almost all other sources have remained constant for 20 years.

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[78] Ritz B, Yu F, Fruin S, Chapa G, Shaw GM, Harris JA. Ambient air pollution and risk of birth defects in Southern California. Am J Epidemiol. 2002 Jan 1;155(1):17-25.
[79] Maisonet M, Bush TJ, Correa A, Jaakkola JJ. Relation between ambient air pollution and low birth weight in the Northeastern United States. Environ Health Perspect. 2001 Jun;109 Suppl 3:351-6.
[80] Ritz B, Wilhelm M, Zhao Y. Air pollution and infant death in southern California, 1989-2000.Pediatrics. 2006 Aug;118(2):493-502.
[81] Conceição GM, Miraglia SG, Kishi HS, Saldiva PH, Singer JM. Air pollution and child mortality: a time-series study in São Paulo, Brazil. Environ Health Perspect. 2001 Jun;109 Suppl 3:347-50.

186. EPA has no control over the total number of CO sources in the US that contribute to these emissions (being the sum of all operating vehicles, combustion power plants, and industrial operations) or the frequency of their operations. Both trends are greatly influenced by trends in local economic activity.

187. Changing meteorological conditions also have a large impact on CO levels in any local jurisdiction, with more CO produced by vehicles in cold winters than mild, more demand for power generation in both colder and hotter weather, and more prevalent wildfires.

188. Past declines in CO emissions and CO levels, therefore, provide no certain predictor of future trends. Both of these gradually declining curves could level off in any year or even rise again, as they have done occasionally over the last 20 years before falling again within another year or two.[82]

189. Given how much room there now is under the CO NAAQS to increase current levels of CO pollution, automakers and other CO-producing industries could decide to save millions by switching to less expensive and less efficient CO control technologies.

190. As a result of changing economic and/or meteorological conditions, 8-hour average CO levels could rise by 400% in most local jurisdictions (from 2 to 9ppm) without violating the CO NAAQS. The 1-hour average could rise over 700% (from under 5ppm to 35ppm).

191. In contrast to the many EE studies that have found statistically significant risks for various serious adverse outcomes (including death) consistently associated with increases in outdoor average CO of just 0.5 to 1ppm, EPA's position that 8-hour average CO exposures up to 9ppm year-round would not trigger any significant adverse effects in any sensitive population is not supported by any studies of any kind, epidemiological or otherwise.

192. EPA's CO NAAQS provides no "margin of safety" since it allows the US population's average CO exposure (and thus also their inhaled dose) to more than quadruple from the current 2ppm.

193. Assuming a linear relationship (which EPA does, citing the results of the Allred CO study as shown in Figure 2 above), such an increase in exposure would result in an approximately four-fold increase in risk.

194. Given that EPA acknowledges the Allred study's pooled data analysis found statistically significant dose-response relationships with no evidence of any threshold, it is arbitrary for EPA to set just such a threshold for the protection of public health at 2% (v)COHb.[83]

195. In contrast, the Administrator could have lowered the CO NAAQS to the maximum of current levels as the CASAC and EPA staff recommended without imposing any additional compliance burdens on any jurisdiction.

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[82] EPA. CO monitoring data accessed 3/21/12 at http://cfpub.epa.gov/eroe/index.cfm?fuseaction=detail.viewInd&lv=list.listbyalpha&r=231329&subtop=341

[83] EPA. Review of National Ambient Air Quality Standards for Carbon Monoxide Federal Register. August 31, 2011 Federal Register76(169):55066-54343

196. This would have at least established that EPA was moving forward in protecting public health from CO exposures by not allowing CO levels—and whatever risks may be associated with them—to rise again to as much as 9ppm average, which would undo all the public health benefits achieved by reductions in CO levels since 1990.

197. Since EPA claims there are no significant risks from chronic CO exposures below 9ppm average, it presumably also believes the decline in outdoor CO levels below 9ppm has not resulted in any public health benefits.

198. But if this is the case, why has EPA adopted other regulations in the last decade designed in part to reduce CO emissions from stationary industrial sources and non-road engines when 8-hour average CO levels were already below 9ppm nationwide? In 2008, EPA adopted new standards for non-road spark-ignition engines, equipment, and vessels that it said would result in "annual reductions of 1.5 million tons of carbon monoxide emissions, with the greatest reductions in situations where there have been problems with individual exposures. This rule will result in substantial benefits to public health and welfare and the environment."[84]

199. Given that EPA recognizes incremental public health benefits in other rules from further reductions of CO emissions, EPA's failure to acknowledge any potential public health benefits from further reductions in the CO NAAQS appears arbitrary and capricious.

I declare under the penalty of perjury that the foregoing is true and correct and was executed this thirtieth day of April, 2012.

Albert Donnay

Albert Donnay

[84] EPA 2008. Final Rule: Control of Emissions from Nonroad Spark-Ignition Engines and Equipment. Federal Register 73(196):59034-59380, October 8, 2008. As described in EPA420-F-08-013, September 2008, accessed online 4/29/2012 at http://www.epa.gov/nonroad/marinesi-equipld/420f08013.htm#7

Attachment A

Studies Presented in Comments Not Addressed by EPA

The following studies cannot be found cited anywhere except particular comments in the record

1. Delfino RJ, Chang J, Wu J, Ren C, Tjoa T, Nickerson B, Cooper D, Gillen DL. Repeated hospital encounters for asthma in children and exposure to traffic-related air pollution near the home. Ann Allergy Asthma Immunol. 2009 Feb;102(2):138-44.

2. Szyszkowicz M. Air pollution and emergency department visits for depression in Edmonton, Canada. Int J Occup Med Environ Health. 2007;20(3):241-5.

3. Abraham NG, Quan S, Mieyal PA, Yang L, Burke-Wolin T, Mingone CJ, Goodman AI, Nasjletti A, Wolin MS. Modulation of cGMP by human HO-1 retrovirus gene transfer in pulmonary microvessel endothelial cells. Am J Physiol Lung Cell Mol Physiol. 2002 Nov;283(5):L1117-24.

4. Abraham NG. Therapeutic applications of human heme oxygenase gene transfer and gene therapy. Curr Pharm Des. 2003;9(30):2513-24. Review.

5. Alam J, Cook JL. How many transcription factors does it take to turn on the heme oxygenase-1 gene? Am J Respir Cell Mol Biol. 2007 Feb;36(2):166-74. Epub 2006 Sep 21. Review.

6. Aono S, Honma Y, Ohkubo K, Tawara T, Kamiya T, Nakajima H. CO sensing and regulation of gene expression by the transcriptional activator CooA. J Inorg Biochem. 2000 Nov;82(1-4):51-6. Review.

7. Aono S. Biochemical and biophysical properties of the CO-sensing transcriptional activator CooA. Acc Chem Res. 2003 Nov;36(11):825-31. Review.

8. Choi YK, Kim CK, Lee H, Jeoung D, Ha KS, Kwon YG, Kim KW, Kim YM. Carbon monoxide promotes VEGF expression by increasing HIF-1alpha protein level via two distinct mechanisms, translational activation and stabilization of HIF-1alpha protein. J Biol Chem. 2010 Oct 15;285(42):32116-25. Epub 2010 Aug 19.

9. Czekaj P, Wiaderkiewicz A, Florek E, Wiaderkiewicz R. Tobacco smoke-dependent changes in cytochrome P450 1A1, 1A2, and 2E1 protein expressions in fetuses, newborns, pregnant rats, and human placenta. Arch Toxicol. 2005 Jan;79(1):13-24.

10. Davidge KS, Sanguinetti G, Yee CH, Cox AG, McLeod CW, Monk CE, Mann BE, Motterlini R, Poole RK. Carbon monoxide-releasing antibacterial molecules target respiration and global transcriptional regulators. J Biol Chem. 2009 Feb 13;284(7):4516-24.

11. Dulak J, Józkowicz A. Carbon monoxide -- a "new" gaseous modulator of gene expression. Acta Biochim Pol. 2003;50(1):31-47. Review.

12. Exner M, Schillinger M, Minar E, Mlekusch W, Schlerka G, Haumer M, Mannhalter C, Wagner O. Heme oxygenase-1 gene promoter microsatellite polymorphism is associated with restenosis after percutaneous transluminal angioplasty. J Endovasc Ther. 2001 Oct;8(5):433-40.

13. Heuser VD, da Silva J, Moriske HJ, Dias JF, Yoneama ML, de Freitas TR. Genotoxicity biomonitoring in regions exposed to vehicle emissions using the comet assay and the micronucleus test in native rodent Ctenomys minutus. Environ Mol Mutagen. 2002;40(4):227-35.
14. Hopkins RO, Weaver LK, Valentine KJ, Mower C, Churchill S, Carlquist J. Apolipoprotein E genotype and response of carbon monoxide poisoning to hyperbaric oxygen treatment. Am J Respir Crit Care Med. 2007 Nov 15;176(10):1001-6. Epub 2007 Aug 16.

15. Katana E, Skoura L, Giakoustidis D, Takoudas D, Malisiovas N, Daniilidis M. Association between the heme oxygenase-1 promoter polymorphism and renal transplantation outcome in Greece. Transplant Proc. 2010 Sep;42(7):2479-85.

16. Ke B, Buelow R, Shen XD, Melinek J, Amersi F, Gao F, Ritter T, Volk HD, Busuttil RW, Kupiec-Weglinski JW. Heme oxygenase 1 gene transfer prevents CD95/Fas ligand-mediated apoptosis and improves liver allograft survival via carbon monoxide signaling pathway. Hum Gene Ther. 2002 Jul 1;13(10):1189-99.

17. Ke B, Shen XD, Buelow R, Melinek J, Amersi F, Gao F, Ritter T, Volk HD, Busuttil RW, Kupiec-Weglinski JW. Heme oxygenase-1 gene transfer prevents CD95/FasL-mediated apoptosis and improves liver allograft survival via carbon monoxide signaling pathway. Transplant Proc. 2002 Aug;34(5):1465-6.

18. Kim YS, Doré S. Catalytically inactive heme oxygenase-2 mutant is cytoprotective. Free Radic Biol Med. 2005 Aug 15;39(4):558-64.

19. Kitamuro T, Takahashi K, Ogawa K, Udono-Fujimori R, Takeda K, Furuyama K, Nakayama M, Sun J, Fujita H, Hida W, Hattori T, Shirato K, Igarashi K, Shibahara S. Bach1 functions as a hypoxia-inducible repressor for the heme oxygenase-1 gene in human cells. J Biol Chem. 2003 Mar 14;278(11):9125-33.

20. Lee SY, Jo HJ, Kim KM, Song JD, Chung HT, Park YC. Concurrent expression of heme oxygenase-1 and p53 in human retinal pigment epithelial cell line. Biochem Biophys Res Commun. 2008 Jan 25;365(4):870-4.

21. Li MH, Jang JH, Na HK, Cha YN, Surh YJ. Carbon monoxide produced by heme oxygenase-1 in response to nitrosative stress induces expression of glutamate-cysteine ligase in PC12 cells via activation of phosphatidylinositol 3-kinase and Nrf2 signaling. J Biol Chem. 2007 Sep 28;282(39):28577-86. Epub 2007 Aug 5.

22. Li P, Elrayess MA, Gomma AH, Palmen J, Hawe E, Fox KM, Humphries SE. The microsatellite polymorphism of heme oxygenase-1 is associated with baseline plasma IL-6 level but not with restenosis after coronary in-stenting. Chin Med J (Engl). 2005 Sep 20;118(18):1525-32.

23. Li YX, Li G, Dong WP, Lu DR, Tan JM. Protection of human islets from induction of apoptosis and improved islet function with HO-1 gene transduction. Chin Med J (Engl). 2006 Oct 5;119(19):1639-45.

24. Lin HH, Lai SC, Chau LY. Heme oxygenase-1/carbon monoxide induces vascular endothelial growth factor expression via p38 kinase-dependent activation of Sp1. J Biol Chem. 2011 Feb 4;286(5):3829-38. Epub 2010 Nov 28.

25. Lin HY, Shen SC, Lin CW, Yang LY, Chen YC. Baicalein inhibition of hydrogen peroxide-induced apoptosis via ROS-dependent heme oxygenase 1 gene expression. Biochim Biophys Acta. 2007 Jul;1773(7):1073-86. Epub 2007 Apr 22.

26. Lin LC, Ho FM, Yen SJ, Wu PY, Hung LF, Huang WJ, Liang YC. Carbon monoxide induces cyclooxygenase-2 expression through MAPKs and PKG in phagocytes. Int Immunopharmacol. 2010 Dec;10(12):1520-5. Epub 2010 Sep 15.

27. Eberhardt M, Powell A, Bonfante G, Rupp V, Guarnaccia JR, Heller M, Reed J. Noninvasive measurement of carbon monoxide levels in ED patients with headache. J Med Toxicol. 2006 Sep;2(3):89-92.

28. Ece A, Gürkan F, Haspolat K, Derman O, Kirbaş G. Passive smoking and expired carbon monoxide concentrations in healthy and asthmatic children. Allergol Immunopathol (Madr). 2000 Sep-Oct;28(5):255-60

29. Andersen ZJ, Olsen TS, Andersen KK, Loft S, Ketzel M, Raaschou-Nielsen O. Association between short-term exposure to ultrafine particles and hospital admissions for stroke in Copenhagen, Denmark. Eur Heart J. 2010 Aug;31(16):2034-40. Epub 2010 Jun 10.

30. Clark NA, Demers PA, Karr CJ, Koehoorn M, Lencar C, Tamburic L, Brauer M. Effect of early life exposure to air pollution on development of childhood asthma. Environ Health Perspect. 2010 Feb;118(2):284-90.

31. Currie J, Neidell M, Schmieder JF. Air pollution and infant health: Lessons from New Jersey. J Health Econ. 2009 May;28(3):688-703. Epub 2009 Feb 27.
32. Dales RE, Cakmak S, Doiron MS. Gaseous air pollutants and hospitalization for respiratory disease in the neonatal period. Environ Health Perspect. 2006 Nov;114(11):1751-4.

33. Giovannini M, Sala M, Riva E, Radaelli G. Hospital admissions for respiratory conditions in children and outdoor air pollution in Southwest Milan, Italy. Acta Paediatr. 2010 Aug;99(8):1180-5. Epub 2010 Mar 6.

34. Klonoff-Cohen H, Lam PK, Lewis A. Outdoor carbon monoxide, nitrogen dioxide, and sudden infant death syndrome. Arch Dis Child. 2005 Jul;90(7):750-3.

35. Lee YL, Su HJ, Sheu HM, Yu HS, Guo YL. Traffic-related air pollution, climate, and prevalence of eczema in Taiwanese school children. J Invest Dermatol. 2008 Oct;128(10):2412-20. Epub 2008 May 1.

36. Morello-Frosch R, Jesdale BM, Sadd JL, Pastor M. Ambient air pollution exposure and full-term birth weight in California. Environ Health. 2010 Jul 28;9:44.

37. Orazzo F, Nespoli L, Ito K, Tassinari D, Giardina D, Funis M, Cecchi A, Trapani C, Forgeschi G, Vignini M, Nosetti L, Pigna S, Zanobetti A. Air pollution, aeroallergens, and emergency room visits for acute respiratory diseases and gastroenteric disorders among young children in six Italian cities. Environ Health Perspect. 2009 Nov;117(11):1780-5. Epub 2009 Aug 13.

38. Zemek R, Szyszkowicz M, Rowe BH. Air Pollution and Emergency Department Visits for Otitis Media: A Case-Crossover Study in Edmonton, Canada. Environ Health Perspect. 2010 Jul 20. [Epub ahead of print]

39. Arbex MA, de Souza Conceição GM, Cendon SP, Arbex FF, Lopes AC, Moysés EP, Santiago SL, Saldiva PH, Pereira LA, Braga AL. Urban air pollution and chronic obstructive pulmonary disease-related emergency department visits. J Epidemiol Community Health. 2009 Oct;63(10):777-83. Epub 2009 May 24.

40. Baja ES, Schwartz JD, Wellenius GA, Coull BA, Zanobetti A, Vokonas PS, Suh HH. Traffic-related air pollution and QT interval: modification by diabetes, obesity, and oxidative stress gene polymorphisms in the normative aging study. Environ Health Perspect. 2010 Jun;118(6):840-6. Epub 2010 Mar 1.
41. Bener A, Dogan M, Shanks NJ. The impact of air pollution on hospital admission for respiratory and cardiovascular diseases in an oil-rich country. East Afr J Public Health. 2009 Aug;6(2):124-7.

42. Bruske I, Hampel R, Socher MM, Rückerl R, Schneider A, Heinrich J, Oberdorster G, Wichmann HE, Peters A. Impact of ambient air pollution on the differential white blood cell count in patients with chronic pulmonary disease. Inhal Toxicol. 2010 Feb;22(3):245-52.

43. Cakmak S, Dales RE, Vidal CB. Air pollution and hospitalization for epilepsy in Chile. Environ Int. 2010 Aug;36(6):501-5. Epub 2010 May 8.

44. Cakmak S, Dales RE, Judek S. Do gender, education, and income modify the effect of air pollution gases on cardiac disease? J Occup Environ Med. 2006 Jan;48(1):89-94.

45. Canova C, Torresan S, Simonato L, Scapellato ML, Tessari R, Visentin A, Lotti M, Maestrelli P. Carbon monoxide pollution is associated with decreased lung function in asthmatic adults. Eur Respir J. 2010 Feb;35(2):266-72. Epub 2009 Aug 13.

46. Chen R, Pan G, Kan H, Tan J, Song W, Wu Z, Xu X, Xu Q, Jiang C, Chen B. Ambient air pollution and daily mortality in Anshan, China: a time-stratified case-crossover analysis. Sci Total Environ. 2010 Nov 15;408(24):6086-91.

47. Cheng MF, Tsai SS, Yang CY. Air pollution and hospital admissions for myocardial infarction in a tropical city: Kaohsiung, Taiwan. J Toxicol Environ Health A. 2009;72(19):1135-40.

48. Cui Y, Zhang ZF, Froines J, Zhao J, Wang H, Yu SZ, Detels R. Air pollution and case fatality of SARS in the People's Republic of China: an ecologic study. Environ Health. 2003 Nov 20;2(1):15.

49. Dales RE, Cakmak S, Vidal CB. Air pollution and hospitalization for headache in Chile. Am J Epidemiol. 2009 Oct 15;170(8):1057-66. Epub 2009 Sep 9.

50. Dennekamp M, Akram M, Abramson MJ, Tonkin A, Sim MR, Fridman M, Erbas B. Outdoor air pollution as a trigger for out-of-hospital cardiac arrests. Epidemiology. 2010 Jul;21(4):494-500.

51. Economopoulou AA, Economopoulos AP. Air pollution in Athens basin and health risk assessment. Environ Monit Assess. 2002 Dec;80(3):277-99.

52. Fung KY, Luginaah I, Gorey KM, Webster G. Air pollution and daily hospitalization rates for cardiovascular and respiratory diseases in London, Ontario. Int J Environ Stud. 2005 Dec 1;62(6):677-685.

53. Hildebrandt K, Rückerl R, Koenig W, Schneider A, Pitz M, Heinrich J, Marder V, Frampton M, Oberdörster G, Wichmann HE, Peters A. Short-term effects of air pollution: a panel study of blood markers in patients with chronic pulmonary disease. Part Fibre Toxicol. 2009 Sep 26;6:25.

54. Kaplan GG, Dixon E, Panaccione R, Fong A, Chen L, Szyszkowicz M, Wheeler A, MacLean A, Buie WD, Leung T, Heitman SJ, Villeneuve PJ. Effect of ambient air pollution on the incidence of appendicitis. CMAJ. 2009 Oct 27;181(9):591-7. Epub 2009 Oct 5.

55. Laumbach RJ, Rich DQ, Gandhi S, Amorosa L, Schneider S, Zhang J, Ohman-Strickland P, Gong J, Lelyanov O, Kipen HM. Acute changes in heart rate variability in subjects with diabetes following a highway traffic exposure. JOccup Environ Med. 2010 Mar;52(3):324-31.

56. Lin CM, Liao CM. Temperature-dependent association between mortality rate and carbon monoxide level in a subtropical city: Kaohsiung, Taiwan. Int J Environ Health Res. 2009 Jun;19(3):163-74.

57. Liu CC, Tsai SS, Chiu HF, Wu TN, Yang CY. Ambient exposure to criteria air pollutants and female lung cancer in Taiwan. Inhal Toxicol. 2008 Feb;20(3):311-7.

58. Norris G, Larson T, Koenig J, Claiborn C, Sheppard L, Finn D. Asthma aggravation, combustion, and stagnant air. Thorax. 2000 Jun;55(6):466-70.

59. Pedersen CB, Raaschou-Nielsen O, Hertel O, Mortensen PB. Air pollution from traffic and schizophrenia risk. Schizophr Res. 2004 Jan 1;66(1):83-5.

60. Pénard-Morand C, Raherison C, Charpin D, Kopferschmitt C, Lavaud F, Caillaud D, Annesi-Maesano I. Long-term exposure to close-proximity air pollution and asthma and allergies in urban children. Eur Respir J. 2010 Jul;36(1):33-40. Epub 2010 Jan 14.

61. Sinclair AH, Edgerton ES, Wyzga R, Tolsma D. A two-time-period comparison of the effects of ambient air pollution on outpatient visits for acute respiratory illnesses. J Air Waste Manag Assoc. 2010 Feb;60(2):163-75.

62. Son JY, Bell ML, Lee JT. Individual exposure to air pollution and lung function in Korea: spatial analysis using multiple exposure approaches. Environ Res. 2010 Nov;110(8):739-49. Epub 2010 Sep 15.

63. Steinvil A, Fireman E, Kordova-Biezuner L, Cohen M, Shapira I, Berliner S, Rogowski O. Environmental air pollution has decremental effects on pulmonary function test parameters up to one week after exposure. Am J Med Sci. 2009 Oct;338(4):273-9.

64. Stieb DM, Smith-Doiron M, Brook JR, Burnett RT, Dann T, Mamedov A, Chen Y. Air pollution and disability days in Toronto: results from the national population health survey. Environ Res. 2002 Jul;89(3):210-9.

65. Stieb DM, Szyszkowicz M, Rowe BH, Leech JA. Air pollution and emergency department visits for cardiac and respiratory conditions: a multi-city time-series analysis. Environ Health. 2009 Jun 10;8:25.

66. Szyszkowicz M, Rowe BH, Colman I. Air pollution and daily emergency department visits for depression. Int J Occup Med Environ Health. 2009;22(4):355-62.

67. Szyszkowicz M, Willey JB, Grafstein E, Rowe BH, Colman I. Air pollution and emergency department visits for suicide attempts in Vancouver, Canada. Environ Health Insights. 2010 Oct 15;4:79-86.

68. Szyszkowicz M. Ambient air pollution and daily emergency department visits for headache in Ottawa, Canada. Headache. 2008 Jul;48(7):1076-81. Epub 2008 Jan 24.

69. Chen YH, Chau LY, Chen JW, Lin SJ. Serum bilirubin and ferritin levels link heme oxygenase-1 gene promoter polymorphism and susceptibility to coronary artery disease in diabetic patients. Diabetes Care. 2008 Aug;31(8):1615-20. Epub 2008 Apr 28.

70. Chen YH, Chau LY, Lin MW, Chen LC, Yo MH, Chen JW, Lin SJ. Heme oxygenase-1 gene promotor microsatellite polymorphism is associated with angiographic restenosis after coronary stenting. Eur Heart J. 2004 Jan;25(1):39-47.

71. Chen YH, Lin SJ, Lin MW, Tsai HL, Kuo SS, Chen JW, Charng MJ, Wu TC, Chen LC, Ding YA, Pan WH, Jou YS, Chau LY. Microsatellite polymorphism in promoter of heme oxygenase-1 gene is associated with susceptibility to coronary artery disease in type 2 diabetic patients. Hum Genet. 2002 Jul;111(1):1-8. Epub 2002 Jun 19.

72. Andersson JA, Uddman R, Cardell LO. Increased carbon monoxide levels in the nasal airways of subjects with a history of seasonal allergic rhinitis and in patients with upper respiratory tract infection. Clin Exp Allergy. 2002 Feb;32(2):224-7.

73. Antczak A, Kharitonov SA, Montuschi P, Gorski P, Barnes PJ. Inflammatory response to sputum induction measured by exhaled markers. Respiration. 2005 Nov-Dec;72(6):594-9. Epub 2005 Jul 1.

74. Antuni JD, Kharitonov SA, Hughes D, Hodson ME, Barnes PJ. Increase in exhaled carbon monoxide during exacerbations of cystic fibrosis. Thorax. 2000 Feb;55(2):138-42.

75. Antus B, Horváth I. Exhaled nitric oxide and carbon monoxide in respiratory diseases. J Breath Res. 2007 Dec;1(2):024002. Epub 2007 Dec 6.

76. Babusikova E, Jesenak M, Durdik P, Dobrota D, Banovcin P. Exhaled carbon monoxide as a new marker of respiratory diseases in children. J Physiol Pharmacol. 2008 Dec;59 Suppl 6:9-17. Review.

77. Baum M, Schiff E, Kreiser D, Dennery PA, Stevenson DK, Rosenthal T, Seidman DS. End-tidal carbon monoxide measurements in women with pregnancy-induced hypertension and preeclampsia. Am J Obstet Gynecol. 2000 Oct;183(4):900-3.

78. Beck-Ripp J, Latzin P, Griese M. Exhaled carbon monoxide is not flow dependent in children with cystic fibrosis and asthma. Eur J Med Res. 2004 Nov 29;9(11):518-22.

79. Biernacki WA, Kharitonov SA, Barnes PJ. Exhaled carbon monoxide in patients with lower respiratory tract infection. Respir Med. 2001 Dec;95(12):1003-5.

80. Chatkin G, Chatkin JM, Aued G, Petersen GO, Jeremias ET, Thiesen FV. Evaluation of the exhaled carbon monoxide levels in smokers with COPD. J Bras Pneumol. 2010 Jun;36(3):332-8. English, Portuguese.

81. Cheng S, Lyass A, Massaro JM, O'Connor GT, Keaney JF Jr, Vasan RS. Exhaled carbon monoxide and risk of metabolic syndrome and cardiovascular disease in the community. Circulation. 2010 Oct 12;122(15):1470-7. Epub 2010 Sep 27.

82. Chow S, Campbell C, Sandrini A, Thomas PS, Johnson AR, Yates DH. Exhaled breath condensate biomarkers in asbestos-related lung disorders. Respir Med. 2009 Aug;103(8):1091-7. Epub 2009 Jun 10.

83. Ciarleglio G, Refini RM, Pieroni MG, Martino VA, Bargagli E, Rottoli P, Sestini P. Exhaled carbon monoxide in sarcoidosis. Sarcoidosis Vasc Diffuse Lung Dis. 2008 Sep;25(1):46-50.

84. Cope KA, Solga SF, Hummers LK, Wigley FM, Diehl AM, Risby TH. Abnormal exhaled ethane concentrations in scleroderma. Biomarkers. 2006 Jan-Feb;11(1):70-84.

85. Dunning MB 3rd, Woehlck HJ. Exhaled CO after surgery: a consequence of postoperative narcotics? Anesth Analg. 2005 Mar;100(3):896; author reply 896.

86. Gajdócsy R, Horváth I. Exhaled carbon monoxide in airway diseases: from research findings to clinical relevance. J Breath Res. 2010 Dec;4(4):047102. Epub 2010 Nov 30.

87. Gomez C, Berlin I, Marquis P, Delcroix M. Expired air carbon monoxide concentration in mothers and their spouses above 5 ppm is associated with decreased fetal growth. Prev Med. 2005 Jan;40(1):10-5.

88. Grover RS, Kumar R. Exhaled carbon monoxide levels: as a marker of clinical severity and control of asthma. J Asthma. 2008 Oct;45(8):677-80.

89. Hanta I, Kocabas A, Olgunus O, Satar S, Seydaoglu G. Does the expired-air carbon monoxide level reflect the severity of inflammation in COPD? Bratisl Lek Listy. 2007;108(6):255-8.

90. Harrison CM, Andersen CC. Exhaled breath measures of inflammation: are they useful in neonatal chronic lung disease? Arch Dis Child Fetal Neonatal Ed. 2005 Jan;90(1):F6-10. Review.

91. lyashi M, Takahashi T, Morimatsu H, Fujii H, Taga N, Mizobuchi S, Matsumi M, Katayama H, Yokoyama M, Taniguchi M, Morita K. Increased carbon monoxide concentration in exhaled air after surgery and anesthesia. Anesth Analg. 2004

92. Herschel M, Karrison T, Wen M, Caldarelli L, Baron B. Evaluation of the direct antiglobulin (Coombs') test for identifying newborns at risk for hemolysis as determined by end-tidal carbon monoxide concentration (ETCOc); and comparison of the Coombs' test with ETCOc for detecting significant jaundice. J Perinatol. 2002 Jul-Aug;22(5):341-7.

93. Hirano K, Sato Y, Kobayashi T, Yamamoto S, Nakatsuka H, Oya H, Kato T, Watanabe T, Kameyama H, Hatakeyama K. Carbon monoxide hemoglobin and bilirubin metabolism in small-for-size graft in adult living-related liver transplantation. Transplant Proc. 2003 Feb;35(1):410-1.

94. Hirano K, Sato Y, Kobayashi T, Yamamoto S, Nakatsuka H, Oya H, Kato T, Watanabe T, Kameyama H, Hatakeyama K. Carbon monoxide hemoglobin and metabolism in adult living-related liver transplantation. Hepatogastroenterology. 2003 Nov-Dec;50(54):1745-8.

95. Horváth I, Loukides S, Wodehouse T, Csiszér E, Cole PJ, Kharitonov SA, Barnes PJ. Comparison of exhaled and nasal nitric oxide and exhaled carbon monoxide levels in bronchiectatic patients with and without primary ciliary dyskinesia. Thorax. 2003 Jan;58(1):68-72. Erratum in: Thorax. 2004 Jun;59(6):543.

96. Alehan F, Erol I, Onay OS. Cerebral palsy due to nonlethal maternal carbon monoxide intoxication. Birth Defects Res A Clin Mol Teratol. 2007 Aug;79(8):614-6.

97. Antón M, Alcaraz A, Rey C, Concha A, Fernández J. Acute hydrocephalus in carbon monoxide poisoning. Acta Paediatr. 2000 Mar;89(3):361-4.

98. Aubard Y, Magne I. Carbon monoxide poisoning in pregnancy. BJOG. 2000 Jul;107(7):833-8. Review.

99. Augustine JJ. The whole family's sick. A little girl's illness leads to the discovery of a lethal threat. EMS Mag. 2008 May;37(5):36, 38.

100. Asirdizer M, Yavuz MS, Albek E, Cantürk G. Infant and adolescent deaths in Istanbul due to home accidents. Turk J Pediatr. 2005 Apr-Jun;47(2):141-9.

101. Campbell TA, Collins KA. Pediatric toxicologic deaths: a 10-year retrospective study. Am J Forensic Med Pathol. 2001 Jun;22(2):184-7.

102. Chesney ML. Carbon monoxide poisoning in the pediatric population. Air Med J. 2002 Nov-Dec;21(6):10-3. Review.

103. Cho CH, Chiu NC, Ho CS, Peng CC. Carbon monoxide poisoning in children. Pediatr Neonatol. 2008 Aug;49(4):121-5.

104. Chou KJ, Fisher JL, Silver EJ. Characteristics and outcome of children with carbon monoxide poisoning with and without smoke exposure referred for hyperbaric oxygen therapy. Pediatr Emerg Care. 2000 Jun;16(3):151-5. \

105. Cousar JL, Lai Y, Marco CD, Bayir H, Adelson PD, Janesko-Feldman KL, Kochanek PM, Clark RS. Heme oxygenase 1 in cerebrospinal fluid from infants and children after severe traumatic brain injury. Dev Neurosci. 2006;28(4-5):342-7.

106. 2023: Erkal S, Safak S. An evaluation of the poisoning accidents encountered in children aged 0-6 years in Kirikkale. Turk J Pediatr. 2006 Oct-Dec;48(4):294-300.

107. Gandini C, Castoldi AF, Candura SM, Priori S, Locatelli C, Butera R, Bellet C, Manzo L. Cardiac damage in pediatric carbon monoxide poisoning. J Toxicol Clin Toxicol. 2001;39(1):45-51.

108. Greingor JL, Tosi JM, Ruhlmann S, Aussedat M. Acute carbon monoxide intoxication during pregnancy. One case report and review of the literature. Emerg Med J. 2001 Sep;18(5):399-401. Review.

109. Grant M, Clay B. Accidental carbon monoxide poisoning with severe cardiorespiratory compromise in 2 children. Am J Crit Care. 2002 Mar;11(2):128-31.

110. Gul A, Gungorduk K, Yildirim G, Gedikbasi A, Ceylan Y. Prenatal diagnosis of porencephaly secondary to maternal carbon monoxide poisoning. Arch Gynecol Obstet. 2009 May;279(5):697-700. Epub 2008 Sep 6.

111. Hon KL, Yeung WL, Ho CH, Leung WK, Li AM, Chu WC, Chan YL. Neurologic and radiologic manifestations of three girls surviving acute carbon monoxide poisoning. J Child Neurol. 2006 Sep;21(9):737-41.

112. Knecht KR, Milam S, Wilkinson DA, Fedinec AL, Leffler CW. Time-dependent action of carbon monoxide on the newborn cerebrovascular circulation. Am J Physiol Heart Circ Physiol. 2010 Jul;299(1):H70-5. Epub 2010 Apr 30.

113. Kondo A, Saito Y, Seki A, Sugiura C, Maegaki Y, Nakayama Y, Yagi K, Ohno K. Delayed neuropsychiatric syndrome in a child following carbon monoxide poisoning. Brain Dev. 2007 Apr;29(3):174-7. Epub 2006 Sep 27.

114. Lee C, Robinson P, Chelladurai J. Reversible sensorineural hearing loss. Int J Pediatr Otorhinolaryngol. 2002 Dec 2;66(3):297-301.

115. 6178: Prusakowski MK. A teenage boy with weakness and syncope. Pediatr Emerg Care. 2007 Sep;23(9):673-5.

116. Teksam O, Gumus P, Bayrakci B, Erdogan I, Kale G. Acute cardiac effects of carbon monoxide poisoning in children. Eur J Emerg Med. 2010 Aug;17(4):192-6.

117. 8352: Wilson M, Rosen P. A case of open-air carbon monoxide poisoning in a 10-year-old boy. J Emerg Med. 2001 Oct;21(3):289-90.

118. Yildiz H, Aldemir E, Altuncu E, Celik M, Kavuncuoglu S. A rare cause of perinatal asphyxia: maternal carbon monoxide poisoning. Arch Gynecol Obstet. 2010 Feb;281(2):251-4. Epub 2009 Jun 6.

119. Ziaei S, Nouri K, Kazemnejad A. Effects of carbon monoxide air pollution in pregnancy on neonatal nucleated red blood cells. Paediatr Perinat Epidemiol. 2005 Jan;19(1):27-30.

120. Acland PR,A65 Heaver C. Retrograde amnesia following carbon monoxide poisoning: a case report. Med Sci Law. 2008 Jul;48(3):251-5.

121. Alioglu Z, Boz C, Sari A, Aynaci M. Transient tic disorder following carbon monoxide poisoning. J Neuroradiol. 2004 Jun;31(3):231-3.

122. Aslan S, Uzkeser M, Seven B, Gundogdu F, Acemoglu H, Aksakal E, Varoglu E. The evaluation of myocardial damage in 83 young adults with carbon monoxide poisoning in the East Anatolia region in Turkey. Hum Exp Toxicol. 2006 Aug;25(8):439-46.

123. Baggett MR, Kelly MP, Korenman LM, Ryan LM. Neuropsychological deficits of a U.S. Army pilot following an anoxic event as a function of cardiac arrest. Mil Med. 2003 Sep;168(9):769-71.

124. Bastin C, Linden M, Charnallet A, Denby C, Montaldi D, Roberts N, Andrew M. Dissociation between recall and recognition memory performance in an amnesic patient with hippocampal damage following carbon monoxide poisoning. Neurocase. 2004 Aug;10(4):330-44.

125. Benignus VA, Coleman TG. Simulations of exercise and brain effects of acute exposure to carbon monoxide in normal and vascular-diseased persons. Inhal Toxicol. 2010 Apr;22(5):417-26.

126. Bledsoe BE. The heart dangers of CO. Understanding cardiovascular risks to responders from CO exposure. JEMS. 2007 Dec;32(12):54-9.

127. Borron SW, Arias JC. Carbon monoxide-induced status epilepticus in an adult. J Burn Care Res. 2008 May-Jun;29(3):559.

128. Bourgeois JA. Amnesia after carbon monoxide poisoning. Am J Psychiatry. 2000 Nov;157(11):1884-5.

129. Brown KL, Wilson RF, White MT. Carbon monoxide-induced status epilepticus in an adult. J Burn Care Res. 2007 May-Jun;28(3):533-6.

130. Chamberland DL, Wilson BD, Weaver LK. Transient cardiac dysfunction in acute carbon monoxide poisoning. Am J Med. 2004 Oct 15;117(8):623-5.

131. Chambers CA, Hopkins RO, Weaver LK, Key C. Cognitive and affective outcomes of more severe compared to less severe carbon monoxide poisoning. Brain Inj. 2008 May;22(5):387-95. Erratum in: Brain Inj. 2008 Dec;22(13-14):1038.

132. Chan GM. Carbon monoxide poisoning, myocardial injury, and mortality. JAMA. 2006 Jun 14;295(22):2601; author reply 2602.

133. Chang CC, Lee YC, Chang WN, Chen SS, Lui CC, Chang HW, Liu WL, Wang YL. Damage of white matter tract correlated with neuropsychological deficits in carbon monoxide intoxication after hyperbaric oxygen therapy. J Neurotrauma. 2009 Aug;26(8):1263-70.

134. Chen SH, Huang SH, Chang WN, Lui CC, Huang CW, Lin YT, Chang CC. Heterotopic ossification as a complication of carbon monoxide intoxication. Acta Neurol Taiwan. 2010 Jun;19(2):120-4.

135. Choi IS. Parkinsonism after carbon monoxide poisoning. Eur Neurol. 2002;48(1):30-3.

136. Denniston A. Carbon monoxide poisoning and the eye. J R Soc Med. 2001 Aug;94(8):425-6.

137. Dileo PA, Tucciarone M, Castro ER, Guerrero M. Late stent thrombosis secondary to carbon monoxide poisoning. Cardiovasc Revasc Med. 2011 Jan-Feb;12(1):56-8. Epub 2010 Oct 20.

138. Duenas-Laita A, Mena-Martín FJ, Roquelai-Ruiz P, Gil-Simon P, Barrio-Andrés J, Martin-Escudero JC. Ischemic colitis associated with acute carbon monoxide poisoning. Clin Toxicol (Phila). 2008 Sep;46(8):780-1.

139. Dueñas-Laita A, Burillo Puzte G, Nogué Xarau S, Ruiz Mambrilla M.Cardiovascular manifestations of carbon monoxide poisoning. J Am Coll Cardiol. 2006 Feb 7;47(3):690-1; author reply 691. Epub 2006 Jan 18.

140. El Khashab M, Nejat F. Hemorrhagic cerebral infarction in carbon monoxide poisoning: a case report. Cases J. 2009 Jan 29;2:96.

141. Fan HC, Wang AC, Lo CP, Chang KP, Chen SJ. Damage of cerebellar white matter due to carbon monoxide poisoning: a case report. Am J Emerg Med. 2009 Jul;27(6):757.e5-7.

142. Fechter LD, Chen GD, Rao D, Larabee J. Predicting exposure conditions that facilitate the potentiation of noise-induced hearing loss by carbon monoxide. Toxicol Sci. 2000 Dec;58(2):315-23.

143. Fielding J, Lang W, White OB. Carbon monoxide poisoning: impact on ocular motility. Cogn Behav Neurol. 2010 Dec;23(4):256-61.

144. Finelli PF, DiMario FJ Jr. Hemorrhagic infarction in white matter following acute carbon monoxide poisoning. Neurology. 2004 Sep 28;63(6):1102-4.

145. Fineschi V, Agricola E, Baroldi G, Bruni G, Cerretani D, Mondillo S, Parolini M, Turillazzi E. Myocardial findings in fatal carbon monoxide poisoning: a human and experimental morphometric study. Int J Legal Med. 2000;113(5):276-82.

146. Fowler PB. Parkinsonism secondary to carbon monoxide poisoning. J R Soc Med. 2000 Jan;93(1):53.

147. Gale SD, Hopkins RO. Effects of hypoxia on the brain: neuroimaging and neuropsychological findings following carbon monoxide poisoning and obstructive sleep apnea. J Int Neuropsychol Soc. 2004 Jan;10(1):60-71.

148. Gale SD, Hopkins RO, Weaver LK, Bigler ED, Booth EJ, Blatter DD. MRI, quantitative MRI, SPECT, and neuropsychological findings following carbon monoxide poisoning. Brain Inj. 1999 Apr;13(4):229-43.

149. Gandini C, Castoldi AF, Candura SM, Locatelli C, Butera R, Priori S, Manzo L. Carbon monoxide cardiotoxicity. J Toxicol Clin Toxicol. 2001;39(1):35-44. Review.

150. García A, Maestro I. Reversible motor and sensory peripheral neuropathy in a patient following acute carbon monoxide intoxication. Electromyogr Clin Neurophysiol. 2005 Jan-Feb;45(1):19-21.

151. Gottfried JA, Chatterjee A. Carbon monoxide-mediated hippocampal injury. Neurology. 2001 Jul 10;57(1):17.

152. Hampson NB. Survival following cardiac arrest associated with carbon monoxide poisoning. Resuscitation. 2009 Sep;80(9):1082; author reply 1082-3. Epub 2009 Jul 14.

153. Han ST, Bhopale VM, Thom SR. Xanthine oxidoreductase and neurological sequelae of carbon monoxide poisoning. Toxicol Lett. 2007 Apr 25;170(2):111-5. Epub 2007 Feb 20.

154. He H, Gao Y, Li C, Wang G, Yao L, Fang J, Gao T. Cutaneous blistering secondary to acute carbon-monoxide intoxication. Clin Exp Dermatol. 2007 Jan;32(1):129-31. Epub 2006 Jul 27.

155. Henry CR, Satran D, Lindgren B, Adkinson C, Nicholson CI, Henry TD. Myocardial injury and long-term mortality following moderate to severe carbon monoxide poisoning. JAMA. 2006 Jan 25;295(4):398-402.

156. Henry TD, Lesser JR, Satran D. Myocardial fibrosis from severe carbon monoxide poisoning detected by cardiac magnetic resonance imaging. Circulation. 2008 Aug 12;118(7):792.

157. Herman LY. Re: "Carbon monoxide poisoning presenting as an afebrile seizure.". Pediatr Neurol. 2001 Mar;24(3):245.

158. Hopkins RO, Fearing MA, Weaver LK, Foley JF. Basal ganglia lesions following carbon monoxide poisoning. Brain Inj. 2006 Mar;20(3):273-81. Review.

159. Hopkins RO, Woon FL. Neuroimaging, cognitive, and neurobehavioral outcomes following carbon monoxide poisoning. Behav Cogn Neurosci Rev. 2006 Sep;5(3):141-55. Review.

160. Hsiao CL, Kuo HC, Huang CC. Delayed encephalopathy after carbon monoxide intoxication--long-term prognosis and correlation of clinical manifestations and neuroimages. Acta Neurol Taiwan. 2004 Jun;13(2):64-70.

161. Hsu PC, Lin TH, Su HM, Lee HC, Huang CH, Lai WT, Sheu SH. Acute carbon monoxide poisoning resulting in ST elevation myocardial infarction: a rare case report. Kaohsiung J Med Sci. 2010 May;26(5):271-5.

162. Ihara M, Fukuyama H, Lee T, Takao S, Kohara N, Shibasaki H. Delayed synaptic dysfunction of association cortices in carbon monoxide intoxication. Ann Neurol. 2001 Dec;50(6):829-30.

163. Jan M, Panjrath G, Jain D. Transient myocardial dysfunction after smoke inhalation. Int J Cardiol. 2007 Jan 18;114(3):e96-9. Epub 2006 Oct 18.

164. Jang WI, Park JH. Transient left ventricular systolic dysfunction associated with carbon monoxide toxicity. J Cardiovasc Ultrasound. 2010 Mar;18(1):12-5. Epub 2010 Mar 31.

165. Jasper BW, Hopkins RO, Duker HV, Weaver LK. Affective outcome following carbon monoxide poisoning: a prospective longitudinal study. Cogn Behav Neurol. 2005 Jun;18(2):127-34.

166. Johnson CD. Carbon monoxide toxicity with neurological and cardiac complications. Bol Asoc Med P R. 2005 Oct-Dec;97(4):315-22.

167. 3545: Jones K, Kinsella GJ, Ong B, Scheinkestel C. Supervisory attentional control following carbon monoxide poisoning. J Int Neuropsychol Soc. 2004 Oct;10(6):843-50.

168. Kahan ES, Martin UJ, Spungen S, Ciccolella D, Criner GJ. Chronic cough and dyspnea in ice hockey players after an acute exposure to combustion products of a faulty ice resurfacer. Lung. 2007 Jan-Feb;185(1):47-54. Epub 2007 Feb 9.

169. Kalay N, Ozdogru I, Cetinkaya Y, Eryol NK, Dogan A, Gul I, Inanc T, Ikizceli I, Oguzhan A, Abaci A. Cardiovascular effects of carbon monoxide poisoning. Am J Cardiol. 2007 Feb 1;99(3):322-4. Epub 2006 Nov 29.

170. Karakurum B, Karataş M, Giray S, Tan M, Yildirim T. Partial recovery from cortical blindness following carbon monoxide intoxication. Int J Neurosci. 2005 Jan;115(1):143-7.

171. Katirci Y, Kandis H, Aslan S, Kirpinar I. Neuropsychiatric disorders and risk factors in carbon monoxide intoxication. Toxicol Ind Health. 2010 Nov 18. [Epub ahead of print]

172. Kesler SR, Hopkins RO, Blatter DD, Edge-Booth H, Bigler ED. Verbal memory deficits associated with fornix atrophy in carbon monoxide poisoning. J Int Neuropsychol Soc. 2001 Jul;7(5):640-6.

173. Kim JH, Chang KH, Song IC, Kim KH, Kwon BJ, Kim HC, Kim JH, Han MH. Delayed encephalopathy of acute carbon monoxide intoxication: diffusivity of cerebral white matter lesions. AJNR Am J Neuroradiol. 2003 Sep;24(8):1592-7.

174. Ko SB, Ahn TB, Kim JM, Kim Y, Jeon BS. A case of adult onset tic disorder following carbon monoxide intoxication. Can J Neurol Sci. 2004 May;31(2):268-70.

175. Kobayashi A, Ando A, Tagami N, Kitagawa M, Kawai E, Akioka M, Arai E, Nakatani T, Nakano S, Matsui Y, Matsumura M. Severe optic neuropathy caused by dichloromethane inhalation. J Ocul Pharmacol Ther. 2008 Dec;24(6):607-12.

176. Ku BD, Shin HY, Kim EJ, Park KC, Seo SW, Na DL. Secondary mania in a patient with delayed anoxic encephalopathy after carbon monoxide intoxication. J Clin Neurosci. 2006 Oct;13(8):860-2. Epub 2006 Aug 28. PubMed PMID=16935513.

177. Kwon OY, Chung SP, Ha YR, Yoo IS, Kim SW. Delayed postanoxic encephalopathy after carbon monoxide poisoning. Emerg Med J. 2004 Mar;21(2):250-1. Review.

178. Lakhani R, Bleach N. Carbon monoxide poisoning: an unusual cause of dizziness. J Laryngol Otol. 2010 Oct;124(10):1103-5. Epub 2010 Apr 14.

179. Lam SP, Fong SY, Kwok A, Wong T, Wing YK. Delayed neuropsychiatric impairment after carbon monoxide poisoning from burning charcoal. Hong Kong Med J. 2004 Dec;10(6):428-31.

180. Larner AJ. Delayed motor and visual complications after attempted suicide. Lancet. 2005 Nov 19;366(9499):1826.

181. Lassinger BK, Kwak C, Walford RL, Jankovic J. Atypical parkinsonism and motor neuron syndrome in a Biosphere 2 participant: a possible complication of chronic hypoxia and carbon monoxide toxicity? Mov Disord. 2004 Apr;19(4):465-9.

182. Lee HF, Mak SC, Chi CS, Hung DZ. Hyperbaric oxygen for carbon monoxide poisoning-induced delayed neuropsychiatric sequelae. Zhonghua Yi Xue Za Zhi (Taipei). 2001 May;64(5):310-4.

183. Lee MS, Lyoo CH, Choi YH. Primary progressive freezing gait in a patient with CO-induced parkinsonism. Mov Disord. 2010 Jul 30;25(10):1513-5.

184. Lee WK, Yu ZH, Lee CC. Delayed neurological sequelae after carbon monoxide poisoning. Aust N Z J Psychiatry. 2008 May;42(5):430.

185. Leikin JB, Wills BK. Long-term psychiatric consequences from carbon monoxide exposure: progression of endogenous cause or toxicant effect? Crit Care Med. 2009 Jun;37(6):2116-8.

186. Liang CS, Chou MK, Yang FW. Delayed-onset diurnal bruxism, psychic akinesia and depression after carbon monoxide poisoning: a case report. Gen Hosp Psychiatry. 2011 Jan-Feb;33(1):82.e9-10. Epub 2010 Sep 20.

187. Lo CP, Chen SY, Lee KW, Chen WL, Chen CY, Hsueh CJ, Huang GS. Brain injury after acute carbon monoxide poisoning: early and late complications. AJR Am J Roentgenol. 2007 Oct;189(4):W205-11. Review.

188. Lynch RM. Is there an evolution in the epidemiology and follow-up of carbon monoxide poisoning victims? Eur J Emerg Med. 2000 Sep;7(3):249.

189. Mori T, Nagai K. Carbon-monoxide poisoning presenting as an afebrile seizure. Pediatr Neurol. 2000 Apr;22(4):330-1.

190. Mumma BE, Shellenbarger D, Callaway CW, Katz KD, Guyette FX, Rittenberger JC. Neurologic recovery following cardiac arrest due to carbon monoxide poisoning. Resuscitation. 2009 Jul;80(7):835. Epub 2009 May 2.

191. :Muller NG, Gruber O. High-resolution magnetic resonance imaging reveals symmetric bitemporal cortical necrosis after carbon monoxide intoxication. J Neuroimaging. 2001 Jul;11(3):322-5.

192. Ong JR, Hou SW, Shu HT, Chen HT, Chong CF, Chong CF. Diagnostic pitfall: carbon monoxide poisoning mimicking hyperventilation syndrome. Am J Emerg Med. 2005 Nov;23(7):903-4.

193. Onvlee-Dekker IM, De Vries AC, Ten Harkel AD. Carbon monoxide poisoning mimicking long-QT induced syncope. Arch Dis Child. 2007 Mar;92(3):244-5.

194. Parenti N, Binetti N, Lenzi T. "Reversible" left bundle branch block in acute carbon monoxide poisoning. Intern Emerg Med. 2006;1(2):172-3.

195. Park S, Choi IS. Chorea following acute carbon monoxide poisoning. Yonsei Med J. 2004 Jun 30;45(3):363-6. Review.

196. Parkinson RB, Hopkins RO, Cleavinger HB, Weaver LK, Victoroff J, Foley JF, Bigler ED. White matter hyperintensities and neuropsychological outcome following carbon monoxide poisoning. Neurology. 2002 May 28;58(10):1525-32. Review.

197. Perez A, Johnson-Arbor K, McKay CA. Carbon monoxide poisoning, myocardial injury, and mortality. JAMA. 2006 Jun 14;295(22):2601; author reply 2602.

198. Pitts S. 3 hyperbaric oxygen treatments reduced cognitive sequelae of acute carbon monoxide poisoning. ACP J Club. 2003 May-Jun;138(3):67.

199. Porter SS, Hopkins RO, Weaver LK, Bigler ED, Blatter DD. Corpus callosum atrophy and neuropsychological outcome following carbon monoxide poisoning. Arch Clin Neuropsychol. 2002 Feb;17(2):195-204.

200. Prockop LD. Carbon monoxide brain toxicity: clinical, magnetic resonance imaging, magnetic resonance spectroscopy, and neuropsychological effects in 9 people. J Neuroimaging. 2005 Apr;15(2):144-9.

201. Quinn DK, McGahee SM, Politte LC, Duncan GN, Cusin C, Hopwood CJ, Stern TA. Complications of carbon monoxide poisoning: a case discussion and review of the literature. Prim Care Companion J Clin Psychiatry. 2009;11(2):74-9.

202. Radwan CM. CO poisoning mimics flu. RN. 2009 Apr;72(4):49.

203. Raj RS, Abdurahiman P, Jose J. Delayed syndrome in carbon monoxide poisoning. J Assoc Physicians India. 2006 Dec;54:955-6.

204. 6262: Ramsey PS, Meyer LM, Ramin KD, Heise RH. Delayed postpartum hemorrhage: a rare presentation of carbon monoxide poisoning. Am J Obstet Gynecol. 2001 Jan;184(2):243-4.

205. Rao DB, Fechter LD. Increased noise severity limits potentiation of noise induced hearing loss by carbon monoxide. Hear Res. 2000 Dec;150(1-2):206-14.

206. Razavi ME, Khalife M. Carbon Monoxide Poisoning: A Patient with Bilateral Internuclear Ophthalmoplegia and Exotropia. J Pediatr Ophthalmol Strabismus. 2009 Jun 25:1-4. doi: 10.3928/01913913-20090616-12. [Epub ahead of print]

207. 6300: Razzaq M, Dumbala S, Moudgil SS. Neurological picture. Sudden deafness due to carbon monoxide poisoning. J Neurol Neurosurg Psychiatry. 2010 Jun;81(6):658.

208. Reed MD, Barrett EG, Campen MJ, Divine KK, Gigliotti AP, McDonald JD, Seagrave JC, Mauderly JL, Seilkop SK, Swenberg JA. Health effects of subchronic inhalation exposure to gasoline engine exhaust. Inhal Toxicol. 2008 Oct;20(13):1125-43.

209. 6343: Ren X, Dorrington KL, Robbins PA. Respiratory control in humans after 8 h of lowered arterial PO2, hemodilution, or carboxyhemoglobinemia. J Appl Physiol. 2001 Apr;90(4):1189-95.

210. Rhine DJ, Best T. Hyperbaric oxygen therapy in carbon monoxide poisoning: effects on neurological sequelae. CJEM. 2000 Jan;2(1):22-4.

211. Richardson RS, Noyszewski EA, Saltin B, González-Alonso J. Effect of mild carboxy-hemoglobin on exercising skeletal muscle: intravascular and intracellular evidence. Am J Physiol Regul Integr Comp Physiol. 2002 Nov;283(5):R1131-9.

212. Rissanen E, Paavilainen T, Virta J, Marttila RJ, Rinne JO, Airas L. Carbon monoxide poisoning-induced nigrostriatal dopaminergic dysfunction detected using positron emission tomography (PET). Neurotoxicology. 2010 Aug;31(4):403-7. Epub 2010 Mar 24.

213. Roberts L, Bailes J, Dedhia H, Zikos A, Singh A, McDowell D, Failinger C, Biundo R, Petrick J, Carpenter J. Surviving a mine explosion. J Am Coll Surg. 2008 Aug;207(2):276-83. Epub 2008 May 19.

214. Roohi F, Kula RW, Mehta N. Twenty-nine years after carbon monoxide intoxication. Clin Neurol Neurosurg. 2001 Jul;103(2):92-5.

215. Satran D, Henry CR, Adkinson C, Nicholson CI, Bracha Y, Henry TD. Cardiovascular manifestations of moderate to severe carbon monoxide poisoning. J Am Coll Cardiol. 2005 May 3;45(9):1513-6.

216. Seet RC, Wilder-Smith EP, Lim EC. Hemorrhagic leukoencephalopathy following acute carbon monoxide poisoning. Eur J Neurol. 2008 Jun;15(6):e49-50.

217. Senol MG, Yildiz S, Ersanli D, Uzun G, Gumus T, Narin Y, Ozkan S, Ayata A. Carbon monoxide-induced cortical visual loss: treatment with hyperbaric oxygen four years later. Med Princ Pract. 2009;18(1):67-9. Epub 2008 Dec 4.

218. Sevinc A, Savli H, Atmaca H. An interesting cause of pulmonary emboli: acute carbon monoxide poisoning. Clin Appl Thromb Hemost. 2005 Jul;11(3):353-7.

219. Shahbaz Hassan M, Ray J, Wilson F. Carbon monoxide poisoning and sensorineural hearing loss. J Laryngol Otol. 2003 Feb;117(2):134-7.

220. Shprecher D, Mehta L. The syndrome of delayed post-hypoxic leukoencephalopathy. NeuroRehabilitation. 2010;26(1):65-72.

221. Sohn YH, Jeong Y, Kim HS, Im JH, Kim JS. The brain lesion responsible for parkinsonism after carbon monoxide poisoning. Arch Neurol. 2000 Aug;57(8):1214-8.

222. Song IU, Chung SW. Chorea as the first neurological symptom of delayed encephalopathy after carbon monoxide intoxication. Intern Med. 2010;49(11):1037-9. Epub 2010 Jun 1.

223. Townsend CL, Maynard RL. Effects on health of prolonged exposure to low concentrations of carbon monoxide. Occup Environ Med. 2002 Oct;59(10):708-11. Review.

224. Subhaschandra S, Jatishwor W, Suraj T. Isolated symmetrical bilateral basal ganglia T2 hyperintensity in carbon monoxide poisoning. Ann Indian Acad Neurol. 2008 Oct;11(4):251-3.

225. Sung PS, Yu CY, Lin TS. Asymmetrical delayed encephalopathy after acute CO intoxication: a case report. Neurotoxicology. 2010 Jan;31(1):161-3. Epub 2009 Dec 23.

226. Sungur M, Güven M. Rhabdomyolysis due to carbon monoxide poisoning. Clin Nephrol. 2001 Apr;55(4):336-7.

227. 7454: Swank G, Jain AC, Morise AP, Schmidt S. Carbon monoxide poisoning: a case report of reversible cardiormyopathy. W V Med J. 2004 Nov-Dec;100(6):228-31.

228. Tanindi A, Yalcin R. Misdiagnosis of carbon monoxide intoxication in a patient with known coronary artery disease--a case report and review of cardiovascular effects of carbon monoxide poisoning. West Indian Med J. 2009 Nov;58(5):485-7. Review.

229. Tapeantong T, Poungvarin N. Delayed encephalopathy and cognitive sequelae after acute carbon monoxide poisoning: report of a case and review of the literature. J Med Assoc Thai. 2009 Oct;92(10):1374-9. Review.

230. Tawackoli W, Chen GD, Fechter LD. Disruption of cochlear potentials by chemical asphyxiants. Cyanide and carbon monoxide. Neurotoxicol Teratol. 2001 Mar-Apr;23(2):157-65.

231. Terajima K, Igarashi H, Hirose M, Matsuzawa H, Nishizawa M, Nakada T. Serial assessments of delayed encephalopathy after carbon monoxide poisoning using magnetic resonance spectroscopy and diffusion tensor imaging on 3.0T system. Eur Neurol. 2008;59(1-2):55-61. Epub 2007 Oct 4.

232. Thom SR, Bhopale VM, Fisher D, Zhang J, Gimotty P. Delayed neuropathology after carbon monoxide poisoning is immune-mediated. Proc Natl Acad Sci U S A. 2004 Sep 14;101(37):13660-5. Epub 2004 Sep 1.

233. Tofighi R, Tillmark N, Daré E, Aberg AM, Larsson JE, Ceccatelli S. Hypoxia-independent apoptosis in neural cells exposed to carbon monoxide in vitro. Brain Res. 2006 Jul 7;1098(1):1-8. Epub 2006 Jun 13.

234. Tucciarone M, Dileo PA, Castro ER, Guerrero M. Myocardial infarction secondary to carbon monoxide poisoning: an uncommon presentation of a common condition. Case report and review of the literature. Am J Ther. 2009 Sep-Oct;16(5):462-5.

235. Uemura K, Harada K, Sadamitsu D, Tsuruta R, Takahashi M, Aki T, Yasuhara M, Maekawa T, Yoshida K. Apoptotic and necrotic brain lesions in a fatal case of carbon monoxide poisoning. Forensic Sci Int. 2001 Feb 15;116(2-3):213-9.

236. Vacchiano G, Torino R. Carbon-monoxide poisoning, behavioural changes and suicide: an unusual industrial accident. J Clin Forensic Med. 2001 Jun;8(2):86-92.

237. Varol E, Ozaydin M, Aslan SM, Doğan A, Altinbaş A. A rare cause of myocardial infarction: acute carbon monoxide poisoning. Anadolu Kardiyol Derg. 2007 Sep;7(3):322-3.

238. Wang P, Zeng T, Chi ZF. Recovery of cognitive dysfunction in a case of delayed encephalopathy of carbon monoxide poisoning after treatment with donepezil hydrochloride. Neurol India. 2009 Jul-Aug;57(4):481-2.

239. Wang P, Zeng T, Zhang CL, Gao XC, Liu Z, Xie KQ, Chi ZF. Lipid peroxidation was involved in the memory impairment of carbon monoxide-induced delayed neuron damage. Neurochem Res. 2009 Jul;34(7):1293-8. Epub 2009 Feb 6.

240. Weaver LK, Hopkins RO. Hemorrhagic infarction in white matter following acute carbon monoxide poisoning. Neurology. 2005 Mar 22;64(6):1101; author reply 1101.

241. Webber AP. Recurrent cardiac failure of environmental origin. J R Soc Med. 2003 Sep;96(9):458-9.

242. Wu CT, Huang JL, Hsia SH. Acute carbon monoxide poisoning with severe cardiopulmonary compromise: a case report. Cases J. 2009 Jan 14;2(1):52.

243. Yamazaki Y, Yamada A. Delayed encephalopathy after carbon monoxide intoxication. Intern Med. 2008;47(11):1071-2. Epub 2008 Jun 2.

244. Yanagawa Y, Saitoh D, Sakamoto T, Okada Y. Unfavorable outcome of burn patients with neuropsychiatric disorders. Tohoku J Exp Med. 2005 Mar;205(3):241-5.

245. Yang HJ, Jeon BS. Selective cerebellar degeneration following carbon monoxide poisoning. AJNR Am J Neuroradiol. 2011 Feb;32(2):E39. Epub 2010 Dec 16.

246. Yanir Y, Shupak A, Abramovich A, Reisner SA, Lorber A. Cardiogenic shock complicating acute carbon monoxide poisoning despite neurologic and metabolic recovery. Ann Emerg Med. 2002 Oct;40(4):420-4.

247. Yildirim C, Günay N, Büyükaslan H, Küçükdurmaz Z, Bozkurt S. A case of carbon monoxide poisoning with thrombus in the heart: a case report. Inhal Toxicol. 2005 Dec 15;17(14):797-801.

248. Yiqun Y, Xue L, Yanrong X, Yanping F. Impairment of cardiac function by acute carbon monoxide poisoning. Chin Med Sci J. 2002 Dec;17(4):257.

249. Zahger D, Slutzky O, Almog Y. Severe reversible left ventricular dysfunction induced by carbon monoxide intoxication. Am J Emerg Med. 2002 Oct;20(6):572-3. PubMed PMID=12369040.

250. Abraham NG, Cao J, Sacerdoti D, Li X, Drummond G. Heme oxygenase: the key to renal function regulation. Am J Physiol Renal Physiol. 2009 Nov;297(5):F1137-52. Epub 2009 Jul 1. Review.

251. Abraham NG, Kappas A. Pharmacological and clinical aspects of heme oxygenase. Pharmacol Rev. 2008 Mar;60(1):79-127. Epub 2008 Mar 6. Review.

252. Abraham NG, Kappas A. Heme oxygenase and the cardiovascular-renal system. Free Radic Biol Med. 2005 Jul 1;39(1):1-25. Epub 2005 Mar 30. Review.

253. Abraham NG, Kushida T, McClung J, Weiss M, Quan S, Lafaro R, Darzynkiewicz Z, Wolin M. Heme oxygenase-1 attenuates glucose-mediated cell growth arrest and apoptosis in human microvessel endothelial cells. Circ Res. 2003 Sep 19;93(6):507-14. Epub 2003 Aug 21.

254. Abraham NG, Quan S, Mieyal PA, Yang L, Burke-Wolin T, Mingone CJ, Goodman AI, Nasjletti A, Wolin MS. Modulation of cGMP by human HO-1 retrovirus gene transfer

in pulmonary microvessel endothelial cells. Am J Physiol Lung Cell Mol Physiol. 2002 Nov;283(5):L1117-24.

255. Abraham NG. Therapeutic applications of human heme oxygenase gene transfer and gene therapy. Curr Pharm Des. 2003;9(30):2513-24. Review.

256. Alam J. Heme oxygenase-1: past, present, and future. Antioxid Redox Signal. 2002 Aug;4(4):559-62.

257. Alcaraz MJ, Fernández P, Guillén MI. Anti-inflammatory actions of the heme oxygenase-1 pathway. Curr Pharm Des. 2003;9(30):2541-51. Review.

258. Andersson KE. Neurotransmission and drug effects in urethral smooth muscle. Scand J Urol Nephrol Suppl. 2001;(207):26-34; discussion 106-25. Review.

259. Ascenzi P, Bocedi A, Leoni L, Visca P, Zennaro E, Milani M, Bolognesi M. CO sniffing through heme-based sensor proteins. IUBMB Life. 2004 Jun;56(6):309-15. Review.

260. Balla J, Vercellotti GM, Jeney V, Yachie A, Varga Z, Eaton JW, Balla G. Heme, heme oxygenase and ferritin in vascular endothelial cell injury. Mol Nutr Food Res. 2005 Nov;49(11):1030-43. Review.

261. Balla J, Vercellotti GM, Jeney V, Yachie A, Varga Z, Jacob HS, Eaton JW, Balla G. Heme, heme oxygenase, and ferritin: how the vascular endothelium survives (and dies) in an iron-rich environment. Antioxid Redox Signal. 2007 Dec;9(12):2119-37. Review.

262. Balla J, Vercellotti GM, Nath K, Yachie A, Nagy E, Eaton JW, Balla G. Haem, haem oxygenase and ferritin in vascular endothelial cell injury. Nephrol Dial Transplant. 2003 Jul;18 Suppl 5:v8-12. Review.

263. Barañano DE, Ferris CD, Snyder SH. Atypical neural messengers. Trends Neurosci. 2001 Feb;24(2):99-106. Review.

264. Barañano DE, Snyder SH. Neural roles for heme oxygenase: contrasts to nitric oxide synthase. Proc Natl Acad Sci U S A. 2001 Sep 25;98(20):10996-1002. Review.

265. Bauer I, Pannen BH. Bench-to-bedside review: Carbon monoxide--from mitochondrial poisoning to therapeutic use. Crit Care. 2009;13(4):220. Epub 2009 Aug 14. Review.

266. Bauer M, Bauer I. Heme oxygenase-1: redox regulation and role in the hepatic response to oxidative stress. Antioxid Redox Signal. 2002 Oct;4(5):749-58. Review.

267. Bauer M, Huse K, Settmacher U, Claus RA. The heme oxygenase-carbon monoxide system: regulation and role in stress response and organ failure. Intensive Care Med. 2008 Apr;34(4):640-8. Epub 2008 Feb 20. Review.

268. Bilban M, Haschemi A, Wegiel B, Chin BY, Wagner O, Otterbein LE. Heme oxygenase and carbon monoxide initiate homeostatic signaling. J Mol Med. 2008 Mar;86(3):267-79. Epub 2007 Nov 22. Review.

269. Boehning D, Snyder SH. Novel neural modulators. Annu Rev Neurosci. 2003;26:105-31. Review.

270. Branco LG, Bicego KC, Carnio EC, Pittman QJ. Gaseous neurotransmitters and their role in anapyrexia. Front Biosci (Elite Ed). 2010 Jun 1;2:948-60. Review.

271. Brusko TM, Wasserfall CH, Agarwal A, Kapturczak MH, Atkinson MA. An integral role for heme oxygenase-1 and carbon monoxide in maintaining peripheral tolerance by CD4+CD25+ regulatory T cells. J Immunol. 2005 May 1;174(9):5181-6. Review.

272. Bach FH. Carbon monoxide: from the origin of life to molecular medicine. Trends Mol Med. 2006 Aug;12(8):348-50. Epub 2006 Jul 10.

273. Calabrese V, Butterfield DA, Scapagnini G, Stella AM, Maines MD. Redox regulation of heat shock protein expression by signaling involving nitric oxide and carbon monoxide: relevance to brain aging, neurodegenerative disorders, and longevity. Antioxid Redox Signal. 2006 Mar-Apr;8(3-4):444-77. Review.

274. Carter EP, Garat C, Imamura M. Continual emerging roles of HO-1: protection against airway inflammation. Am J Physiol Lung Cell Mol Physiol. 2004 Jul;287(1):L24-5. Review.

275. Chang EF, Claus CP, Vreman HJ, Wong RJ, Noble-Haeusslein LJ. Heme regulation in traumatic brain injury: relevance to the adult and developing brain. J Cereb Blood Flow Metab. 2005 Nov;25(11):1401-17. Review.

276. Chen YH, Yet SF, Perrella MA. Role of heme oxygenase-1 in the regulation of blood pressure and cardiac function. Exp Biol Med (Maywood). 2003 May;228(5):447-53. Review.

277. Chin BY, Otterbein LE. Carbon monoxide is a poison... to microbes! CO as a bactericidal molecule. Curr Opin Pharmacol. 2009 Aug;9(4):490-500. Epub 2009 Jul 27. Review.

278. Chodorowski Z, Sein Anand J, Nowak-Banasik L, Szydłowska M, Klimek J, Kaletha K. Carbon monoxide--a regulator of vascular tone in hypoxia? Przegl Lek. 2005;62(6):438-40. Review.

279. Christova T, Diankova Z, Setchenska M. Heme oxygenase--carbon monoxide signalling pathway as a physiological regulator of vascular smooth muscle cells. Acta Physiol Pharmacol Bulg. 2000;25(1):9-17. Review.

280. Chung HT, Choi BM, Kwon YG, Kim YM. Interactive relations between nitric oxide (NO) and carbon monoxide (CO): heme oxygenase-1/CO pathway is a key modulator in NO-mediated antiapoptosis and anti-inflammation. Methods Enzymol. 2008;441:329-38. Review.

281. Chung HT, Pae HO, Cha YN. Role of heme oxygenase-1 in vascular disease. Curr Pharm Des. 2008;14(5):422-8. Review.

282. Coceani F. Carbon monoxide in vasoregulation: the promise and the challenge. Circ Res. 2000 Jun 23;86(12):1184-6. Review.

283. Cohen RS, Wong RJ, Stevenson DK. Understanding neonatal jaundice: a perspective on causation. Pediatr Neonatol. 2010 Jun;51(3):143-8. Review.

284. Cooper CE, Brown GC. The inhibition of mitochondrial cytochrome oxidase by the gases carbon monoxide, nitric oxide, hydrogen cyanide and hydrogen sulfide: chemical mechanism and physiological significance. J Bioenerg Biomembr. 2008 Oct;40(5):533-9. Epub 2008 Oct 7. Review.

285. Courtney AE, Maxwell AP. Heme oxygenase 1: does it have a role in renal cytoprotection? Am J Kidney Dis. 2008 Apr;51(4):678-90. Epub 2008 Mar 6. Review.

286. Cutajar MC, Edwards TM. Evidence for the role of endogenous carbon monoxide in memory processing. J Cogn Neurosci. 2007 Apr;19(4):557-62. Review.

287. Davidge KS, Motterlini R, Mann BE, Wilson JL, Poole RK. Carbon monoxide in biology and microbiology: surprising roles for the "Detroit perfume". Adv Microb Physiol. 2009;56:85-167. Epub 2009 Nov 26. Review.

288. Derbyshire ER, Marletta MA. Biochemistry of soluble guanylate cyclase. Handb Exp Pharmacol. 2009;(191):17-31. Review.

289. Deshane J, Wright M, Agarwal A. Heme oxygenase-1 expression in disease states. Acta Biochim Pol. 2005;52(2):273-84. Epub 2005 May 31. Review.

290. Domek-Łopacińska K, Strosznajder JB. Cyclic GMP metabolism and its role in brain physiology. J Physiol Pharmacol. 2005 Mar;56 Suppl 2:15-34. Review.

291. Doré S. Decreased activity of the antioxidant heme oxygenase enzyme: implications in ischemia and in Alzheimer's disease. Free Radic Biol Med. 2002 Jun 15;32(12):1276-82. Review.

292. Drennan CL, Doukov TI, Ragsdale SW. The metalloclusters of carbon monoxide dehydrogenase/acetyl-CoA synthase: a story in pictures. J Biol Inorg Chem. 2004 Jul;9(5):511-5. Epub 2004 Jun 18. Review.

293. Dulak J, Deshane J, Jozkowicz A, Agarwal A. Heme oxygenase-1 and carbon monoxide in vascular pathobiology: focus on angiogenesis. Circulation. 2008 Jan 15;117(2):231-41. Review.

294. Dulak J, Loboda A, Jozkowicz A. Effect of heme oxygenase-1 on vascular function and disease. Curr Opin Lipidol. 2008 Oct;19(5):505-12. Review.

295. Durante W. Targeting heme oxygenase-1 in vascular disease. Curr Drug Targets. 2010 Dec;11(12):1504-16. Review. PubMed PMID'=20704550; PubMed Central

296. Durante W. Heme oxygenase-1 in growth control and its clinical application to vascular disease. J Cell Physiol. 2003 Jun;195(3):373-82. Review.

297. Durante W. Carbon monoxide and bile pigments: surprising mediators of vascular function. Vasc Med. 2002 Aug;7(3):195-202. Review.

298. Eaton WA, Henry ER, Hofrichter J, Bettati S, Viappiani C, Mozzarelli A. Evolution of allosteric models for hemoglobin. IUBMB Life. 2007 Aug-Sep;59(8-9):586-99. Review.

299. Ferenbach DA, Kluth DC, Hughes J. Hemeoxygenase-1 and renal ischaemia-reperfusion injury. Nephron Exp Nephrol. 2010;115(3):e33-7. Epub 2010 Apr 24. Review.

300. Ferrándiz ML, Devesa I. Inducers of heme oxygenase-1. Curr Pharm Des. 2008;14(5):473-86. Review.

301. Fukuto JM, Collins MD. Interactive endogenous small molecule (gaseous) signaling: implications for teratogenesis. Curr Pharm Des. 2007;13(29):2952-78. Review.

302. Ghosh S, Gal J, Marczin N. Carbon monoxide: endogenous mediator, potential diagnostic and therapeutic target. Ann Med. 2010;42(1):1-12. Review.

303. Gibbons SJ, Farrugia G. The role of carbon monoxide in the gastrointestinal tract. J Physiol. 2004 Apr 15;556(Pt 2):325-36. Epub 2004 Feb 6. Review.

304. Hartsfield CL. Cross talk between carbon monoxide and nitric oxide. Antioxid Redox Signal. 2002 Apr;4(2):301-7. Review.

305. Hill-Kapturczak N, Chang SH, Agarwal A. Heme oxygenase and the kidney. DNA Cell Biol. 2002 Apr;21(4):307-21. Review.

306. Hoekstra KA, Godin DV, Cheng KM. Protective role of heme oxygenase in the blood vessel wall during atherogenesis. Biochem Cell Biol. 2004 Jun;82(3):351-9. Review.

307. Hoenicka M, Schmid C. Cardiovascular effects of modulators of soluble guanylyl cyclase activity. Cardiovasc Hematol Agents Med Chem. 2008 Oct;6(4):287-301. Review.

308. Hoetzel A, Schmidt R. Regulatory role of anesthetics on heme oxygenase-1. Curr Drug Targets. 2010 Dec;11(12):1495-503. Review.

309. Hoetzel A, Dolinay T, Schmidt R, Choi AM, Ryter SW. Carbon monoxide in sepsis. Antioxid Redox Signal. 2007 Nov;9(11):2013-26. Review.

310. Hou S, Heinemann SH, Hoshi T. Modulation of BKCa channel gating by endogenous signaling molecules. Physiology (Bethesda). 2009 Feb;24:26-35. Review.

311. Idriss NK, Blann AD, Lip GY. Hemoxygenase-1 in cardiovascular disease. J Am Coll Cardiol. 2008 Sep 16;52(12):971-8. Review.

312. Igarashi K, Sun J. The heme-Bach1 pathway in the regulation of oxidative stress response and erythroid differentiation. Antioxid Redox Signal. 2006 Jan-Feb;8(1-2):107-18. Review.

313. Immenschuh S, Schröder H. Heme oxygenase-1 and cardiovascular disease. Histol Histopathol. 2006 Jun;21(6):679-85. Review.

314. Jarmi T, Agarwal A. Heme oxygenase and renal disease. Curr Hypertens Rep. 2009 Feb;11(1):56-62. Review.

315. Jin Y, Choi AM. Cytoprotection of heme oxygenase-1/carbon monoxide in lung injury. Proc Am Thorac Soc. 2005;2(3):232-5. Review.

316. Johnson RA, Johnson FK. The effects of carbon monoxide as a neurotransmitter. Curr Opin Neurol. 2000 Dec;13(6):709-13. Review.

317. Kaczorowski DJ, Zuckerbraun BS. Carbon monoxide: medicinal chemistry and biological effects. Curr Med Chem. 2007;14(25):2720-5. Review.

318. Jozkowicz A, Was H, Dulak J. Heme oxygenase-1 in tumors: is it a false friend? Antioxid Redox Signal. 2007 Dec;9(12):2099-117. Review.

319. Kajimura M, Fukuda R, Bateman RM, Yamamoto T, Suematsu M. Interactions of multiple gas-transducing systems: hallmarks and uncertainties of CO, NO, and H2S gas biology. Antioxid Redox Signal. 2010 Jul 15;13(2):157-92. Review.

320. Kashiba M, Kajimura M, Goda N, Suematsu M. From O2 to H2S: a landscape view of gas biology. Keio J Med. 2002 Mar;51(1):1-10. Review.

321. Kasparek MS, Linden DR, Kreis ME, Sarr MG. Gasotransmitters in the gastrointestinal tract. Surgery. 2008 Apr;143(4):455-9. Epub 2008 Jan 30. Review.

322. Kikuchi G, Yoshida T, Noguchi M. Heme oxygenase and heme degradation. Biochem Biophys Res Commun. 2005 Dec 9;338(1):558-67. Epub 2005 Aug 15. Review.

323. Kim HP, Ryter SW, Choi AM. CO as a cellular signaling molecule. Annu Rev Pharmacol Toxicol. 2006;46:411-49. Review.

324. Koehler RC, Traystman RJ. Cerebrovascular effects of carbon monoxide. Antioxid Redox Signal. 2002 Apr;4(2):279-90. Review.

325. Lee CY, Yen MH. Nitric oxide and carbon monoxide, collaborative and competitive regulators of hypertension. Chang Gung Med J. 2009 Jan-Feb;32(1):12-21. Review.

326. Li L, Moore PK. An overview of the biological significance of endogenous gases: new roles for old molecules. Biochem Soc Trans. 2007 Nov;35(Pt 5):1138-41. Review.

327. Li L, Hsu A, Moore PK. Actions and interactions of nitric oxide, carbon monoxide and hydrogen sulphide in the cardiovascular system and in inflammation--a tale of three gases! Pharmacol Ther. 2009 Sep;123(3):386-400. Epub 2009 May 30. Review.

328. Li Volti G, Sacerdoti D, Di Giacomo C, Barcellona ML, Scacco A, Murabito P, Biondi A, Basile F, Gazzolo D, Abella R, Frigiola A, Galvano F. Natural heme oxygenase-1 inducers in hepatobiliary function. World J Gastroenterol. 2008 Oct 28;14(40):6122-32. Review.

329. Li Volti G, Rodella LF, Di Giacomo C, Rezzani R, Bianchi R, Borsani E, Gazzolo D, Motterlini R. Role of carbon monoxide and biliverdin in renal ischemia/reperfusion injury. Nephron Exp Nephrol. 2006;104(4):e135-9. Epub 2006 Aug 10. Review.

330. Li X, Bazer FW, Gao H, Jobgen W, Johnson GA, Li P, McKnight JR, Satterfield MC, Spencer TE, Wu G. Amino acids and gaseous signaling. Amino Acids. 2009 May;37(1):65-78. Epub 2009 Mar 6. Review.

331. Lorigados CB, Soriano FG, Szabo C. Pathomechanisms of myocardial dysfunction in sepsis. Endocr Metab Immune Disord Drug Targets. 2010 Sep 1;10(3):274-84. Review.

332. Lyall F. Development of the utero-placental circulation: the role of carbon monoxide and nitric oxide in trophoblast invasion and spiral artery transformation. Microsc Res Tech. 2003 Mar 1;60(4):402-11. Review.

333. Maines MD. The heme oxygenase system: update 2005. Antioxid Redox Signal. 2005 Nov-Dec;7(11-12):1761-6. Review.

334. Mancuso C, Perluigi M, Cini C, De Marco C, Giuffrida Stella AM, Calabrese V. Heme oxygenase and cyclooxygenase in the central nervous system: a functional interplay. J Neurosci Res. 2006 Nov 15;84(7):1385-91. Review.

335. Mancuso C. Heme oxygenase and its products in the nervous system. Antioxid Redox Signal. 2004 Oct;6(5):878-87. Review.

336. Mancuso C, Barone E. The heme oxygenase/biliverdin reductase pathway in drug research and development. Curr Drug Metab. 2009 Jul;10(6):579-94. Epub 2009 Jul 14. Review.

337. Marks GS, Brien JF, Nakatsu K. What role does the heme-- heme oxygenase--carbon monoxide system play in vasoregulation? Am J Physiol Regul Integr Comp Physiol. 2003 Sep;285(3):R522-3. Review.

338. Meyer O, Gremer L, Ferner R, Ferner M, Dobbek H, Gnida M, Meyer-Klaucke W, Huber R. The role of Se, Mo and Fe in the structure and function of carbon monoxide dehydrogenase. Biol Chem. 2000 Sep-Oct;381(9-10):865-76. Review.

339. Morse D, Choi AM. Heme oxygenase-1: from bench to bedside. Am J Respir Crit Care Med. 2005 Sep 15;172(6):660-70. Epub 2005 May 18. Review.

340.: Morse D, Choi AM. Heme oxygenase-1: the "emerging molecule" has arrived. Am J Respir Cell Mol Biol. 2002 Jul;27(1):8-16. Review.

341. Morse D, Lin L, Choi AM, Ryter SW. Heme oxygenase-1, a critical arbitrator of cell death pathways in lung injury and disease. Free Radic Biol Med. 2009 Jul 1;47(1):1-12. Epub 2009 Apr 9. Review.

342. Morse D, Sethi J, Choi AM. Carbon monoxide-dependent signaling. Crit Care Med. 2002 Jan;30(1 Suppl):S12-7. Review.

343. Morse D, Sethi J. Carbon monoxide and human disease. Antioxid Redox Signal. 2002 Apr;4(2):331-8. Review.

344. Mustafa AK, Gadalla MM, Snyder SH. Signaling by gasotransmitters. Sci Signal. 2009 Apr 28;2(68):re2. Review.

345. Nagababu E, Rifkind JM. Heme degradation by reactive oxygen species. Antioxid Redox Signal. 2004 Dec;6(6):967-78. Review.

346. Nienhaus K, Nienhaus GU. Searching for neuroglobin's role in the brain. IUBMB Life. 2007 Aug-Sep;59(8-9):490-7. Review.

347. Olson KR, Donald JA. Nervous control of circulation--the role of gasotransmitters, NO, CO, and H2S. Acta Histochem. 2009;111(3):244-56. Epub 2009 Jan 6. Review.

348. Owens EO. Endogenous carbon monoxide production in disease. Clin Biochem. 2010 Oct;43(15):1183-8. Epub 2010 Jul 23. Review.

349. Ozono R. New biotechnological methods to reduce oxidative stress in the cardiovascular system: focusing on the Bach1/heme oxygenase-1 pathway. Curr Pharm Biotechnol. 2006 Apr;7(2):87-93. Review.

350. Perrella MA, Yet SF. Role of heme oxygenase-1 in cardiovascular function. Curr Pharm Des. 2003;9(30):2479-87. Review.

351. Poon HF, Calabrese V, Scapagnini G, Butterfield DA. Free radicals: key to brain aging and heme oxygenase as a cellular response to oxidative stress. J Gerontol A Biol Sci Med Sci. 2004 May;59(5):478-93. Review.

352. Poulos TL. Structural biology of heme monooxygenases. Biochem Biophys Res Commun. 2005 Dec 9;338(1):337-45. Epub 2005 Sep 13. Review.

353. Pryor WA, Houk KN, Foote CS, Fukuto JM, Ignarro LJ, Squadrito GL, Davies KJ. Free radical biology and medicine: it's a gas, man! Am J Physiol Regul Integr Comp Physiol. 2006 Sep;291(3):R491-511. Epub 2006 Apr 20. Review.

354. Pun PB, Lu J, Kan EM, Moochhala S. Gases in the mitochondria. Mitochondrion. 2010 Mar;10(2):83-93. Epub 2009 Dec 22. Review.

355. Raval CM, Lee PJ. Heme oxygenase-1 in lung disease. Curr Drug Targets. 2010 Dec;11(12):1532-40. Review.

356. Ring A, Stremmel W. The hepatic microvascular responses to sepsis. Semin Thromb Hemost. 2000;26(5):589-94. Review.

357. Rivier C. Role of nitric oxide and carbon monoxide in modulating the activity of the rodent hypothalamic-pituitary-adrenal axis. Front Horm Res. 2002;29:15-49. Review.

358. Roberts GP, Thorsteinsson MV, Kerby RL, Lanzilotta WN, Poulos T. CooA: a heme-containing regulatory protein that serves as a specific sensor of both carbon monoxide and redox state. Prog Nucleic Acid Res Mol Biol. 2001;67:35-63. Review.

359. Roberts GP, Kerby RL, Youn H, Conrad M. CooA, a paradigm for gas sensing regulatory proteins. J Inorg Biochem. 2005 Jan;99(1):280-92. Review.

360. Roberts GP, Youn H, Kerby RL. CO-sensing mechanisms. Microbiol Mol Biol Rev. 2004 Sep;68(3):453-73. Review.

361. Ryter SW, Otterbein LE, Morse D, Choi AM. Heme oxygenase/carbon monoxide signaling pathways: regulation and functional significance. Mol Cell Biochem. 2002 May-Jun;234-235(1-2):249-63. Review.

362. Ryter SW, Otterbein LE. Carbon monoxide in biology and medicine. Bioessays. 2004 Mar;26(3):270-80. Review.

363. Schipper HM. Heme oxygenase-1: role in brain aging and neurodegeneration. Exp Gerontol. 2000 Sep;35(6-7):821-30. Review.

364. Schipper HM. Heme oxygenase-1: transducer of pathological brain iron sequestration under oxidative stress. Ann N Y Acad Sci. 2004 Mar;1012:84-93. Review.

365. Schipper HM. Heme oxygenase expression in human central nervous system disorders. Free Radic Biol Med. 2004 Dec 15;37(12):1995-2011. Review.

366. Shamloul R. The potential role of the heme oxygenase/carbon monoxide system in male sexual dysfunctions. J Sex Med. 2009 Feb;6(2):324-33. Review.

367. Shibahara S, Han F, Li B, Takeda K. Hypoxia and heme oxygenases: oxygen sensing and regulation of expression. Antioxid Redox Signal. 2007 Dec;9(12):2209-25. Review.

368. Shibahara S, Kitamuro T, Takahashi K. Heme degradation and human disease: diversity is the soul of life. Antioxid Redox Signal. 2002 Aug;4(4):593-602. Review.

369. Slebos DJ, Ryter SW, Choi AM. Heme oxygenase-1 and carbon monoxide in pulmonary medicine. Respir Res. 2003;4:7. Epub 2003 Aug 7. Review.

370. Snyder SH, Barañano DE. Heme oxygenase: a font of multiple messengers. Neuropsychopharmacology. 2001 Sep;25(3):294-8. Review.

371. Snyder SH, Ferris CD. Novel neurotransmitters and their neuropsychiatric relevance. Am J Psychiatry. 2000 Nov;157(11):1738-51. Review.

372. Soares MP, Usheva A, Brouard S, Berberat PO, Gunther L, Tobiasch E, Bach FH. Modulation of endothelial cell apoptosis by heme oxygenase-1-derived carbon monoxide. Antioxid Redox Signal. 2002 Apr;4(2):321-9. Review.

373. Sorenson JR. Prion diseases: copper deficiency states associated with impaired nitrogen monoxide or carbon monoxide transduction and translocation. J Inorg Biochem. 2001 Dec 1;87(3):125-7. Review.

374. Stec DE, Drummond HA, Vera T. Role of carbon monoxide in blood pressure regulation. Hypertension. 2008 Mar;51(3):597-604. Epub 2008 Jan 22. Review.

375. Stevenson DK, Vreman HJ, Wong RJ, Contag CH. Carbon monoxide and bilirubin production in neonates. Semin Perinatol. 2001 Apr;25(2):85-93. Review.

376. Surh YJ, Kundu JK, Li MH, Na HK, Cha YN. Role of Nrf2-mediated heme oxygenase-1 upregulation in adaptive survival response to nitrosative stress. Arch Pharm Res. 2009 Aug;32(8):1163-76. Epub 2009 Aug 29. Review.

377. Szabo G, Romics L Jr, Frendl G. Liver in sepsis and systemic inflammatory response syndrome. Clin Liver Dis. 2002 Nov;6(4):1045-66, x. Review.

378. Szurszewski JH, Farrugia G. Carbon monoxide is an endogenous hyperpolarizing factor in the gastrointestinal tract. Neurogastroenterol Motil. 2004 Apr;16 Suppl 1:81-5. Review.

379. Takagi T, Naito Y, Uchiyama K, Yoshikawa T. The role of heme oxygenase and carbon monoxide in inflammatory bowel disease. Redox Rep. 2010;15(5):193-201. Review.

380. Takeda A, Itoyama Y, Kimpara T, Zhu X, Avila J, Dwyer BE, Perry G, Smith MA. Heme catabolism and heme oxygenase in neurodegenerative disease. Antioxid Redox Signal. 2004 Oct;6(5):888-94. Review.

381. Tsuchihashi S, Fondevila C, Kupiec-Weglinski JW. Heme oxygenase system in ischemia and reperfusion injury. Ann Transplant. 2004;9(1):84-7. Review.

382. Wagener FA, Volk HD, Willis D, Abraham NG, Soares MP, Adema GJ, Figdor CG. Different faces of the heme-heme oxygenase system in inflammation. Pharmacol Rev. 2003 Sep;55(3):551-71. Epub 2003 Jul 17. Review.

383. Wang CY, Chau LY. Heme oxygenase-1 in cardiovascular diseases: molecular mechanisms and clinical perspectives. Chang Gung Med J. 2010 Jan-Feb;33(1):13-24. Review.

384. Watts RN, Ponka P, Richardson DR. Effects of nitrogen monoxide and carbon monoxide on molecular and cellular iron metabolism: mirror-image effector molecules that target iron. Biochem J. 2003 Feb 1;369(Pt 3):429-40. Review. Erratum in: Biochem J. 2003 Mar 15;730(Pt 3):1111.

385. Wegiel B, Chin BY, Otterbein LE. Inhale to survive, cycle or die? Carbon monoxide and cellular proliferation. Cell Cycle. 2008 May 15;7(10):1379-84. Epub 2008 Mar 11. Review.

386. Bains SK, Foresti R, Howard J, Atwal S, Green CJ, Motterlini R. Human sickle cell blood modulates endothelial heme oxygenase activity: effects on vascular adhesion and reactivity. Arterioscler Thromb Vasc Biol. 2010 Feb;30(2):305-12. Epub 2009 Dec 3.

387. Bak I, Papp G, Turoczi T, Varga E, Szendrei L, Vecsernyes M, Joo F, Tosaki A. The role of heme oxygenase-related carbon monoxide and ventricular fibrillation in ischemic/reperfused hearts. Free Radic Biol Med. 2002 Sep 1;33(5):639-48.

388. Wegiel B, Chin BY, Otterbein LE. Inhale to survive, cycle or die? Carbon monoxide and cellular proliferation. Cell Cycle. 2008 May 15;7(10):1379-84. Epub 2008 Mar 11. Review.

389. Weinberg JB, Lopansri BK, Mwaikambo E, Granger DL. Arginine, nitric oxide, carbon monoxide, and endothelial function in severe malaria. Curr Opin Infect Dis. 2008 Oct;21(5):468-75. Review.

390. Weisiger RA. Carbon monoxide and sepsis: is a toxic gas good for your liver? Gastroenterology. 2001 Apr;120(5):1288-91. Review.

391. Wojas-Pelc A, Marcinkiewicz J. What is a role of haeme oxygenase-1 in psoriasis? Current concepts of pathogenesis. Int J Exp Pathol. 2007 Apr;88(2):95-102. Review.

392. Wunder C, Potter RF. The heme oxygenase system: its role in liver inflammation. Curr Drug Targets Cardiovasc Haematol Disord. 2003 Sep;3(3):199-208. Review.

393. Zhu X, Fan WG, Li DP, Lin MC, Kung H. Heme oxygenase-1 system and gastrointestinal tumors. World J Gastroenterol. 2010 Jun 7;16(21):2633-7. Review.

Addendum C

UNITED STATES COURT OF APPEALS
FOR THE DISTRICT OF COLUMBIA CICUIT

COMMUNITIES FOR A BETTER ENVIRONMENT and WILDEARTH GUARDIANS, Petitioners, v. UNITED STATES ENVIRONMENTAL PROTECTION AGENCY, Respondent.	Case No. 11-1423

DECLARATION OF SHANA LAZEROW IN SUPPORT OF COMMUNITIES FOR A BETTER ENVIRONMENT'S CLAIM OF STANDING

I, Shana Lazerow, do hereby declare as follows:

1. The facts set forth in this declaration are based on my personal knowledge and if called as a witness, I could and would competently testify thereto under oath.

2. I am a staff attorney for Communities for a Better Environment ("CBE").

3. CBE is organized as a 501(c)(3) nonprofit corporation. CBE is a purely charitable organization and has no commercial interests in any of its activities.

4. CBE's mission is to achieve environmental health and justice by building grassroots power in and with communities of color and working-class communities.

5. CBE has thousands of members throughout the state of California. More than 2,700 of CBE's members live, work, or engage with environmental justice issues in urban communities in Northern and Southern California.

6. In particular, CBE has members who live, work, and recreate in and around areas that are impacted or will be impacted by carbon monoxide ("CO").

7. CBE has many members who reside in urban areas heavily affected by CO emissions. Some CBE members reside in areas near heavily-trafficked freeways, including but not limited to Interstate 880 in East Oakland and Interstate 710 in Los Angeles. Other CBE members live near major seaports and airports, and near significant stationary sources of CO emissions. CBE members in these areas are at increased risk from respiratory ailments and other health related issues related to air pollution. These ailments result in reduced ability to participate in school, work, and the pursuit of activities that relate to their membership in CBE. Further, they face a likelihood that their children and grandchildren will be born with lower than normal birth rates and therefore face a lifetime of health and developmental risks.

8. Due to the health effects experienced by CBE members, CBE members are harmed by EPA's decision to maintain the 1971 Primary CO National Ambient Air Quality Standard ("NAAQS").

9. In addition to causing adverse health impacts on CBE members, CO directly and indirectly impacts the greenhouse effect, and consequently, climate change. CBE and its members work to prevent climate change, and the disparate impacts it will have on low-income communities of color.

10. CBE and its members are harmed by the failure of the EPA to establish any secondary National Ambient Air Quality Standard for carbon monoxide. Despite the fact that carbon monoxide adversely affects the global climate, including the wildlife, fish, and plants that depend on a stable and healthy climate, the EPA ultimately decided not to establish any limits on carbon monoxide to protect environmental, or welfare-based, values.

11. On behalf of its members, CBE timely submitted comments on the EPA's proposed rule to retain the NAAQS for CO, raising concerns over the adequacy of the primary standard and the lack of a secondary standard to limit harmful levels of carbon monoxide emissions. According to current scientific data, current carbon monoxide standards fail to limit concentrations of this harmful pollutant such that health and environmental values are sufficiently protected. The

current standards harm CBE and many of its members in a number of ways and the EPA's failure to update these standards perpetuates this harm.

12. A favorable ruling would redress the harms that CBE and its members are experiencing. Cleaner air near roadways and lower emissions will allow CBE's members to live longer, healthier lives. As the organization's members intend to continue to live, work, and recreate in the areas where they currently do, these harms will be ongoing without a favorable ruling.

I declare under the penalty of perjury that the foregoing is true and correct and was executed this thirtieth day of April, 2012.

Shana Lazerow

CERTIFICATE OF SERVICE

I hereby certify that on this 30th day of April, 2012, I served the counsel of record listed below the foregoing **Petitioners' and Petitioner-Intervenor's Opening Brief** by dispatching a hard copy to a third party commercial service for copying and delivery. Counsel of record are:

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Addendum D

**UNITED STATES COURT OF APPEALS
FOR THE DISTRICT OF COLUMBIA CICUIT**

COMMUNITIES FOR A BETTER ENVIRONMENT and WILDEARTH GUARDIANS, Petitioners, v. UNITED STATES ENVIRONMENTAL PROTECTION AGENCY, Respondent.	Case No. 11-1423

DECLARATION OF JEREMY NICHOLS IN SUPPORT OF WILDEARTH GUARDIANS' CLAIM OF STANDING

I, Jeremy Nichols, do hereby declare as follows:

1. The facts set forth in this declaration are based on my personal knowledge and if called as a witness, I could and would competently testify thereto under oath.

2. I reside in Golden, Colorado. Golden is 15 miles west of Denver. It lies within the Denver Metropolitan Area of Colorado, also known as the Denver Metro Area. I work in Downtown Denver. I have lived in the Denver Metropolitan Area for more than eight years.

3. I am a member and employee of WildEarth Guardians. I am the Director of WildEarth Guardians' Climate and Energy Program and have been for

the last four years. I have donated to the organization, and thus have been a member, for the last four years as well.

4. WildEarth Guardians is organized as a 501(c)(3) nonprofit corporation. Guardians is a purely charitable organization and has no commercial interests in any of its activities. WildEarth Guardians has more than 5,000 members, the vast majority of whom live in the American West.

5. Guardians' mission is to protect and restore wildlife, wild rivers, and wild places in the American West. As part of its Climate and Energy Program, WildEarth Guardians works to safeguard clean air, a healthy climate, and other natural values that are needed to promote and sustain vibrant and prosperous communities from the impacts of fossil fuels. I support this mission personally.

6. I am an avid outdoor recreationist. Although I recreate frequently in more remote areas in Colorado and in surrounding states, I frequently bicycle on the extensive bike path system in the Denver Metro Area. For example, I frequently bicycle on the bike paths in the Denver Metro Area that run along the South Platte River, Cherry Creek, Clear Creek, and Bear Creek. I ride my bike on these paths for recreational purposes at least once a month, but usually more frequently, and have done so for the last eight years. I cannot remember the details of every last bike ride, but last week, I rode my bike on the Clear Creek bike path just east of Golden, two weeks ago, I rode my bike on the Bear Creek bike path

west of Denver, and a month ago, I rode my bike on the South Platte River bike path just north of downtown Denver.

7. I enjoy riding my bike on these paths, especially with my nine year-old son. I enjoy the exercise, viewing wildlife and the streams, being outdoors, and being with my son. I intend to continue recreating on these bike paths throughout the foreseeable future.

8. Large portions of these bike paths travel very near some of the busiest roadways in Colorado, including the U.S. Interstate 25 corridor, U.S. Interstate 225 corridor, U.S. Interstate 25/Interstate 70 interchange, U.S. Interstate 270, U.S. Interstate 76, Colorado State Highway 58, and U.S. Highway 285. The Clear Creek bike path, for example, parallels State Highway 58. The Bear Creek bike path parallels U.S. Highway 285 for several miles. The South Platte River bike path parallels Interstate 25 and passes through the Interstate 25 and Interstate 70 corridor.

9. The traffic on these freeways produces air pollution that is often visible (especially in the wintertime), smells, and raises serious concerns over the impacts to my health. I experience this air pollution pretty much every time I ride on bike paths along the creeks and rivers in the Denver Metro Area. It detracts from my enjoyment of my recreational outings. My enjoyment of my recreational outings will continue to be diminished in the future because of this air pollution.

10. This traffic and the associated air pollution diminishes my ability to enjoy the outdoors in the Denver Metro Area. For example, when I ride down the South Platte River bike path, which I have done at least six times a year for the last eight years, the sights, smells, and sounds of air pollution from traffic on Interstate 25, Interstate 70, and Interstate 76, are offensive and worrisome. Although I understand there are many chemicals produced as a result of fossil fuel combustion, I know that carbon monoxide is a large component of the byproduct of combustion. I would have a much more enjoyable ride if this air pollution were curtailed.

11. I intend to continue engaging in outdoor recreation in the Denver Metro Area, including riding my bike along the region's bike paths. My enjoyment will continue to be diminished if this air pollution is not curtailed.

12. My concerns over air pollution near busy roadways are very much validated by the science relied upon by the ("Environmental Protection Agency") EPA in its review of the National Ambient Air Quality Standards for carbon monoxide, which indicates that current levels of carbon monoxide allowed near busy roadways are not protective of public health.

13. I am very aware of the science relied upon by the EPA in its review of the National Ambient Air Quality Standards for carbon monoxide. On behalf of its members, WildEarth Guardians joined in submitted comments on the EPA's

proposed rule to retain the National Ambient Air Quality Standards for carbon monoxide, raising concerns over the adequacy of the primary standard and the lack of a secondary standard to limit harmful levels of carbon monoxide emissions. According to current scientific data, current carbon monoxide standards fail to limit concentrations of this harmful pollutant such that health and environmental values are sufficiently protected. The current standards harm WildEarth Guardians and its members in a number of ways and the EPA's failure to update these standards perpetuates this harm.

14. On a personal level, the EPA's failure to update the carbon monoxide National Ambient air Quality Standards poses a number of harms. Aside from the harm of experiencing the sights, smells, and sounds of carbon monoxide pollution from freeways near where I recreate, the EPA's failure to update its standards poses harm to the environmental values that I enjoy and seek out when I engage in outdoor recreation.

15. For example, despite the EPA's own recognition that carbon monoxide adversely affects the global climate, including the wildlife, fish, and plants that depend on a stable and healthy climate, the EPA ultimately decided not to establish any limits on carbon monoxide to protect environmental, or welfare-based, values. This failure presents concrete harm to myself. For example, while I regularly recreate, I enjoy viewing wildlife, including birds such as Cooper's

hawk, Stellar's jay, and waterfowl such as merganser, bufflehead, and scaup. Data indicates that climate change is adversely affecting populations of a number of bird species, including these birds, whether by destroying their habitat, forcing species to move to different climates in order to survive, or by giving other birds a competitive advantage.

16. The EPA's decision not to adopt a welfare based carbon monoxide standard harms myself and WildEarth Guardians because it fails to protect welfare-based values, including wildlife, from the effects of carbon monoxide on climate change, diminishing my ability to enjoy viewing wildlife and to enjoy my recreational activities.

17. A favorable ruling would redress the harms that myself and WildEarth Guardians will experience. I intend to continue recreating in the Denver Metro Area. In fact, next weekend, I intend to ride along the Clear Creek bike path, which travels next to State Highway 58. Cleaner air near roadways and less emissions that adversely affect the global climate will allow me to better enjoy my outdoor recreational activities. It will also allow WildEarth Guardians to fulfill its conservation mission and ensure that its other members are similarly able to better enjoy their outdoor recreational activities.

I declare under the penalty of perjury that the foregoing is true and correct and was executed this thirtieth day of April 2012.

Jeremy Nichols

CERTIFICATE OF SERVICE

I hereby certify that on this 30th day of April, 2012, I served the counsel of record listed below the foregoing **Petitioners' and Petitioner-Intervenor's Opening Brief** by dispatching a hard copy to a third party commercial service for copying and delivery. Counsel of record are:

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Addendum E

UNITED STATES COURT OF APPEALS
FOR THE DISTRICT OF COLUMBIA CICUIT

COMMUNITIES FOR A BETTER ENVIRONMENT and WILDEARTH GUARDIANS,

Petitioners,

v.

UNITED STATES ENVIRONMENTAL PROTECTION AGENCY,

Respondent.

Case No. 11-1423

DECLARATION OF MAXINE OLIVER-BENSON IN SUPPORT OF COMMUNITIES FOR A BETTER ENVIRONMENT'S CLAIM OF STANDING

I, Maxine Oliver-Benson, do hereby declare as follows:

1. The facts set forth in this declaration are based on my personal knowledge and if called as a witness, I could and would competently testify thereto under oath.

2. I am a member of Communities for a Better Environment. I live at 10481 West Court, which is in the Sobrante Park neighborhood of East Oakland. I have lived in Sobrante Park for 19 years.

3. My part of Sobrante Park is a very diverse community including Asian, Pacific Islander, Latino and African American community members.

4. It is also a part of Alameda County that hosts a wide range of air pollution sources, including mobile sources like Interstate 880 and transit facilities, and stationary sources like chemical companies, metal recyclers and foundries. Oakland International Airport is also located in East Oakland.

5. The combination of these air pollution sources combine to make air quality where I live very poor.

6. I am very worried about the health impacts these pollutants have on my family, my friends and my neighbors. Since I first moved there, seven women who moved in after me contracted cancer. They didn't have cancer when they moved there. Five have since died. Many children in my neighborhood have asthma. Others have diabetes. Lots of them stay out of school because they are sick, and their families can't afford medication to treat their conditions.

7. One of the concerns in my community is low birth weight. It is my understanding that babies who are born too small often die. Those that survive have a hard time as infants. I am aware of scientific studies showing that low birth weight babies are more likely to become obese and have diabetes later in life. I also believe there may be a connection with lung development, cognitive ability and ADHD.

8. I have three great grandnephews who live in the neighborhood at 98th & East 14th Street, in East Oakland. All three were born with low birth weight. One suffers from ADHD and has a heart murmur, another has a brain disease.

9. I have learned that exposing mothers to carbon monoxide while they are pregnant makes it more likely that their children will be born with low birth weight.

10. It is my understanding that the Bay Area meets the current federal standard for carbon monoxide. However, I do not believe that standard is protecting me, my family or my community from carbon monoxide.

11. Poor people and people in my neighborhood cannot afford to buy their own carbon monoxide meters, so they may not even know when carbon monoxide is coming into their homes. I think there should be rules requiring property owners to install and maintain carbon monoxide monitors, just like smoke detectors, to protect lives of the tenants who are ensuring the property owners' livelihoods. That's a small price to pay.

12. If the federal government were to make carbon monoxide standards more protective, I believe my community, and the rest of the Bay Area, would be exposed to less carbon monoxide, and would be able to sleep and live better. This would be a protection for our families.

13. Even if a new standard were one that the Bay Area failed to meet, I would still benefit by having more accurate information so that I could more accurately to assess the risks to me, my family and my community. In addition, I believe that a stricter federal carbon monoxide standard would spur stricter controls on sources of carbon monoxide in and around my community. And this will ensure that my family and my community is provided the same access to healthful air as the property owners who can afford to buy the meters to protect their own families.

I declare under the penalty of perjury that the foregoing is true and correct and was executed this thirtieth day of April, 2012.

Maxine Oliver-Benson

Maxine Oliver-Benson

CERTIFICATE OF SERVICE

I hereby certify that on this 30th day of April, 2012, I served the counsel of record listed below the foregoing **Petitioners' and Petitioner-Intervenor's Opening Brief** by dispatching a hard copy to a third party commercial service for copying and delivery. Counsel of record are:

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CERTIFICATE OF SERVICE

I hereby certify that on this 14th day of May, 2012, I served the counsel of record listed below the foregoing **Petitioners' and Petitioner-Intervenor's Corrected Opening Brief** by dispatching a hard copy to a third party commercial service for copying and delivery. Counsel of record are:

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